ABSTRACT

Title of Dissertation Proposal: THE EFFECT OF TRAINING HABITS ON CUMULATIVE LOAD AND TIBIAL STRESS FRACTURE INJURY RISK IN RUNNERS

Jessica G. Hunter

Dissertation Proposal directed by: Ross H. Miller, Associate Professor, Department of Kinesiology

Running for exercise is beneficial for preventing chronic diseases, but the incidence and prevalence of running related injuries are high, creating a barrier to participation. Traditional research paradigms attribute high running injury rates to anatomical factors, training habits, and high peak loads resulting from gait mechanics. However, the specific mechanisms of tibial stress fracture injuries, a serious running-related injury, and why females are at such high risk for these injuries, are largely unknown. Runners often train at variable running speeds and durations that can affect the accumulation of potentially injurious loads, but until recently, studies on running injuries have mostly considered training habits and mechanical loads separately. Therefore, the purpose of this dissertation was to identify how training factors of running speed, volume, and duration contribute to the loads accumulated by the body in relation to tibial stress fracture injury risk. Specifically, this dissertation consists of three studies which determine i) the cumulative load of two proportions of running speed over a constant distance and average pace of running, ii) how fatigue-related gait adjustments affect the loads accumulated per-kilometer within a single prolonged run, and if there is a relationship between gait adjustments and physiological or cognitive fatigue outcomes; and iii) if fatigue-related changes in running gait affect the model-predicted cumulative damage and probability of tibial stress fracture. In study 1, a combination of slow and fast speeds led to greater estimated cumulative load compared to running at all normal speed. The greater cumulative load resulted from greater loading during slow running compared to fast running. In study 2, runners maintained gait mechanics and cumulative loads throughout an easy run to fatigue. In study 3, the model-predicted cumulative damage and probability of tibial stress fracture injury were similar between hypothetically maintained gait and measured fatigue-adjusted gait conditions. These results suggest running volume and average pace are not sufficient metrics for tracking cumulative load, and fatigue during running is not likely a major injury risk factor. Further, these results suggest that other training factors or individual factors may play a greater role in injury development than running speed, volume, or fatigue.

THE EFFECT OF TRAINING HABITS ON CUMULATIVE LOAD AND TIBIAL STRESS FRACTURE INJURY RISK IN RUNNERS

by

Jessica G. Hunter

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Advisory Committee:
Ross H. Miller, Associate Professor, Chair
Irene S. Davis, Professor
Sushant M. Ranadive, Assistant Professor
Jae Kun Shim, Professor
Norman M. Wereley, Professor

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Chapter 1: Introduction

Running for exercise and leisure has increased in popularity in recent decades, increasing from the 10^{th} most popular sporting activity in 1979 to the number one most popular activity in 2009 (Scheerder & Vos, 2011). The most popular race distance in the United States in 2018 was the 5k, and 59% of the nearly 9 million 5k race registrants were women (Running USA, 2019). Running also has a relatively low barrier of entry; the cost of running shoes generally ranges from ~$50-97 and comfort rather than cost is a sufficient criteria for selection (Clinghan, Arnold, Drew, Cochrane, & Abboud, 2008). In addition to leisure and enjoyment, running as a regular physical activity is beneficial for the prevention of chronic diseases such as hypertension, hypercholesterolemia (Williams, 1997, 2008), diabetes (Williams, 2008), and osteoarthritis (Williams, 2013). Coronary heart disease risk decreased with higher levels of physical activity, and there was no point of diminishing return for those who ran up to 80 km/wk (Williams, 1997). Run/walking as an exercise intervention improved blood sugar, a marker of diabetes, when participants focused on increasing run/walk mileage over 10 weeks, rather than focusing on run/walk time (Morris et al., 2017). From a chronic disease perspective, these results indicate that more running is better. However, incidence and prevalence of running related injuries are high, and injuries create a barrier to continued participation in running for exercise.

Injury incidence and prevalence in novice, recreational runners is as high as 38% (Chan et al., 2018) and 55% (Hespanhol Junior, Costa, Carvalho, & Lopes, 2012), respectively, and injuries come with costs. The overall cost of running injuries is quantified as a combination of direct costs, (money paid for treatment), indirect costs, (lost wages) or in training time lost due to injury (Hespanhol Junior, Huisstede, et al., 2016; Hespanhol Junior, van Mechelen, Postuma, & Verhagen, 2016). Of a sample of participants of a 6-week novice training program, ~26% of runners experienced an injury at a total cost of ~$114,000 or $12 per person (Hespanhol Junior, Huisstede, et al., 2016). For runners preparing for longer race distances over a 6 month training period, this cost was ~$6300 overall and $117 per person (Hespanhol Junior, van Mechelen, et al., 2016). Over 6 months of training, only 26.8% of injuries did not affect training time, and injuries led to a cumulative time loss of 3 days of training (Hespanhol Junior, van Mechelen, et al., 2016). These costs may seem trivial compared to those of major chronic diseases like cardiovascular disease. However the barrier to participation that runners suffering from injuries face prevent them from reaping the health benefits of regular cardiovascular exercise, especially when the injuries are more severe and require long periods of recovery. Injuries requiring cessation of running can also result in negative psychological effects (Chan & Grossman, 1988). Runners who were unable to run for 4 weeks due to injury experienced greater overall psychological distress, including anxiety, depression, confusion, anger and hostility, lower self-esteem, and lower body image compared to active runners (Chan & Grossman, 1988). It is therefore important to improve our understanding of causal risk factors in running injuries, particularly in high-risk populations, and what can be done to reduce these risks.

Runners who are inexperienced and/or female are particularly susceptible to running injuries. Concerning experience, runners with less than 5 years experience and who ran 3 days per week or less were more likely to suffer an injury than those with more experience and/or ran more frequently (Hespanhol Junior et al., 2012). The rate of injuries in novice runners in an 8-13 week training program was 33 per 1000 hours of running (Buist, Bredeweg, Lemmink, Van Mechelen, & Diercks, 2010) compared to only 7.7 per 1000 hours in more experienced recreational runners (Videbæk, Bueno, Nielsen, & Rasmussen, 2015). Concerning gender/sex, females experience a higher rate of injuries than males in most studies (Messier et al., 2018). Females beginning a training program for weight loss and health benefits may be at particularly higher risk of injuries since runners with high body mass index have a higher risk of injury (Malisoux, Nielsen, Urhausen, & Theisen, 2015; Reinking, Austin, & Hayes, 2013; VanDerWorp et al., 2016, 2015). Females also experienced higher rates of tibial stress fractures than males, one of the more serious running-related injuries, at the beginning of a training program (Wentz, Liu, Haymes, & Ilich, 2011), consistent with the estimated risk of tibial stress fractures being highest during the first ~40 days of beginning a running regimen, regardless of mileage or running speed (Edwards, Taylor, Rudolphi, Gillette, & Derrick, 2009, 2010; Taylor, Casolari, & Bignardi, 2004). Identifying the mechanisms for tibial stress fracture injuries in female novice runners is therefore important for this population to maintain and benefit from regular physical activity.

Traditional research paradigms attribute high injury rates in runners in general to anatomical factors such as Q-angle, training habits such as intensity and volume, and high peak values of internal or external mechanical loads. However, the specific mechanisms of tibial stress fracture injuries, and why females are at higher risk for these injuries, are largely unknown. The common belief that women have a wider pelvis and therefore a greater Q-angle than men, and that this contributes to their injury risk, is relatively unsupported. Both male and female cross-country runners with very high and very low Q-angles had higher injury incidence compared to runners with mid-range Q-angles (Rauh, Koepsell, Rivara, Rice, & Margherita, 2007). While females on average have greater Q-angles than males

(Rauh et al., 2007; Weiss, DeForest, Hammond, Schilling, & Ferreira, 2013), groups of male and female runners both had Q-angle ranges from < 10° to ≥ 20° (Rauh et al., 2007). Pelvis width was also similar between male and female runners in absolute width and when normalized to stature (Schache, Blanch, Rath, Wrigley, & Bennell, 2003). Therefore, pelvis width and Q-angle may not explain the higher incidence of injuries in female compared to male runners.

Training errors are another factor often attributed to running injuries, specifically running too much, too fast, or progressing volume or intensity too quickly (Hreljac, 2004). However, the connection between training practices and injury incidence is also unclear. Training volume of injured versus uninjured runners was similar in recreational runners (Hreljac, Marshall, & Hume, 2000) and runners who completed higher weekly running frequency and/or volume suffered less injuries than those who did lower frequency and/or volume running (Malisoux et al., 2015; Saragiotto et al., 2014; Taunton et al., 2003; Van Middelkoop, Kolkman, Van Ochten, Bierma-Zeinstra, & Koes, 2008). In addition, groups of runners following training programs with levels of progression from 10-30% in either volume or intensity had similar injury incidences (Nielsen et al., 2014; Ramskov et al., 2018), although the types of injuries the runners experienced varied based on whether volume or intensity increased more throughout training (Nielsen et al., 2014). Incorporating some proportion of very fast running as interval training (Hespanhol Junior, Pena Costa, & Lopes, 2013) or progressing training by increasing pace rather than volume (Nielsen et al., 2014) appears to have a protective effect on injury development. These results indicate that there may be optimal proportions of various running speeds and volumes for running.

However, specifically what the proportions of running at different speeds should be, and if these proportions vary between runners of different experience levels, is unknown.

High incidence of running injuries is also attributed to “poor” running mechanics in general, and high peak loads specifically. “Peak load” here is typically the greatest value of some kinetic mechanical variable during the stride. There is strong evidence that high peaks loads contribute to the development of various running related in juries (Chan et al., 2018; Davis, Bowser, & Mullineaux, 2016; Davis, Milner, & Hamill, 2004; Gerlach et al., 2005; Hreljac et al., 2000; VanDerWorp, Vrielink, & Bredeweg, 2016). There is also a strong association between high peak loads and tibial stress fracture injuries both retrospectively and prospectively (Chan et al., 2018; Davis et al., 2016; Milner, Ferber, Pollard, Hamill, & Davis, 2006; VanDerWorp et al., 2016). Within-subject peak loads also increase concomitantly with speed (Hamill, Bates, Knutzen, & Sawhill, 1983; Ueda et al., 2016). This association between high peak loads and injury incidence, and high peak loads and fast speeds, contributes to the belief that too much fast running causes injuries. However, when controlling for running speed between injured and uninjured runners, peak loads were similar (Messier et al., 2018), and as previously stated, some proportion of fast running is protective against running injuries. Therefore, attributing running injuries to high peak loads may oversimplify the mechanisms of injury, and limit the ability of current biomechanics research to fully explain the problem. Thus, new research paradigms using materials science concepts of fatigue-failure mechanics are emerging.

Until recently, previous studies on running injuries have mostly considered training habits and mechanical loads separately. However, an interaction between these two factors leading to running injuries is likely (Gallagher & Schall Jr., 2017). Fatigue-failure mechanics considers the exponential relationship between the stresses applied to a material structure, i.e. the peak loads, and the number of loading cycles the structure can withstand before fracturing, i.e. the number of steps (Gallagher & Schall Jr., 2017). The cumulative damage of a material is quantified by considering the various loads applied and the number of loading cycles at each respective load (Gallagher & Schall Jr., 2017). In running this requires consideration of the various speeds a runners uses during training, the proportion of running completed at each speed, and the material properties of the structures being loaded. However, in biological materials this method does not account for remodeling that occurs in response to loading, therefore quantifying the relationship between loads and loading cycles in biological tissues describes the cumulative load rather than cumulative damage (Edwards, 2018). Recent studies applying these concepts to running at different speeds have found that slow running results in higher cumulative loads than fast running over an equal distance (Petersen, Sorensen, & Ostergaard, 2015). However, many runners use a mix of speeds over a training volume rather than a single fast or slow speed. It is unknown how combining different running speeds over a volume of running affects the loads accumulated. In addition, biomechanical studies often measure running mechanics of participants at one moment in time, and then make inferences about how characteristics of their running mechanics affect their risk of injury. However, prolonged running causes modifications in running mechanics, such as step length and peak loads, that may affect the load accumulated throughout a single run or over a volume of running (Maas, De Bie, Vanfleteren, Hoogkamer, & Vanwanseele, 2018; Paquette & Melcher, 2017). Thus far, estimates of cumulative load do not consider the variety of speeds runners use over a volume of training, or the gait modifications associated with prolonged running that may contribute to cumulative load and the development of running related injuries.

Therefore, the overarching purpose of this dissertation research was to identify how training factors of running speed, volume, and duration contribute to the loads accumulated by the body, and affect tibial stress fracture injury risk. To achieve this, the individual studies i) estimated the cumulative load of two proportions of running speed over a constant distance and average pace of running; ii) estimated how fatigue-related gait adjustments affect the loads accumulated per-kilometer within a single prolonged run, and if there is a relationship between gait adjustments and either physiological or cognitive fatigue outcomes; and iii) estimated if fatigue-related gait adjustment affected cumulative damage or the probability of failure of the tibia compared to no effect of fatigue.

More specifically, the purpose of the first study was to compare the vertical average loading rate, peak free moment, and peak axial tibial load between two different proportions of running speed over an equal distance: (i) all distance at a “normal” self-selected speed, and (ii) the same distance split between self-selected “slow” and “fast” speeds such that the average speed equals “normal”. Per-step magnitudes of each load variable and step length are expected to increase concomitantly with speed. It is unclear if load peaks or step lengths are more sensitive to speed, therefore the hypothesis is that 1) that running all distance at normal speed and running the same distance at the same average speed using a combination of slow and fast speed would have similar estimated cumulative VALR, free moment, and tibial load, and 2) that the slow and fast speed would contribute similarly to the total cumulative load of the slow and fast combination.

The purpose of the second study was to compare the cumulative load of the VALR, peak free moment, peak axial tibial load, and peak tibial impact acceleration for each kilometer of a prolonged, sub-threshold run to volitional fatigue. Untrained runners show an increase in cadence and decrease in step length when fatigued (Willson & Kernozek, 1999) but if or how loading variables will change with fatigue is unclear. Therefore, it is expected that runners will maintain step length and peak loads for a portion of the run, after which step length will gradually decrease and peak loads will remain constant, leading to an increase in the per-kilometer cumulative loads. Heart rate and RPE continuously increase during steady-state exercise, while blood lactate accumulation response varies based on exercise intensity (Oyono-Enguelle et al., 1990). Therefore, it is expected that heart rate and RPE will positively correlate with cumulative loads but not per-step loads, and there will be no relationship between blood lactate accumulation and per-step or per-kilometer cumulative load variables.

The purpose of the third study was to model fatigue effects on cumulative damage and probability of tibial stress fracture due to fatigue-related gait adjustments throughout a prolonged run in novice female runners. Fatigue during running has been shown to cause decreases in stride length (Fischer, Storniolo, & Peyré-Tartaruga, 2015; Willson & Kernozek, 1999) and have little effect on ankle moments (Jafarnezhadgero, Alavi-Mehr, & Granacher, 2019). Therefore, the hypothesis is that gait adjustments due to fatigue will increase the cumulative damage and probability of tibial stress fracture injury due to an increase in the number of loading cycles. A secondary purpose was to determine if running longer distance is associated with a greater risk of injury, indicated by an increased probability of failure due to fatigue. The hypothesis is that longer distances will be associated with greater fatigue and therefore a greater probability of failure compared to the non-fatigued condition.

Chapter 2: Literature Review

Running is a popular activity for recreation and health, and has seen a dramatic increase in participation among women in recent decades (Scheerder & Vos, 2011). However, women show a higher risk of tibial stress fracture than men, particularly when beginning a training program with a low level of aerobic fitness (Wentz et al., 2011). The mechanisms of running-related injury are not well understood which limits athletes, coaches, and clinicians from implementing appropriate prevention strategies. Traditional paradigms attributing high peak loads, anatomical factors, and/or training habits to injury development have not consistently explained the high rate of injury in runners (Bredeweg, Kluitenberg, Bessem, & Buist, 2013; Davis et al., 2016; Gerlach et al., 2005; Hreljac et al., 2000). There is general consensus that the running biomechanics field needs new paradigms to better understand and explain the causal mechanisms of running injuries (Bertelsen et al., 2017; Edwards, 2018a; Nigg, Mohr, & Nigg, 2017; Paquette & Miller, 2018).

In one relatively new paradigm, biomechanics research on running-related injury has recently incorporated concepts from materials science in an attempt to determine how loads, training habits, and anthropometrics may interact to lead to running related injury as a mechanical fatigue-failure process (Bertelsen et al., 2017; Gallagher & Schall Jr., 2017). "Fatigue" here refers to the materials science definition of mechanical fatigue (degradation of material properties with cyclical loading) rather than the medical definition more common in exercise science that describes a decline in performance, or performance fatigability. This literature review will examine the factors that contribute to tibial stress fracture injury, one of the more serious running-related injuries, that is often cast as a mechanical fatigue problem.

Since there is little prospective data on this particular injury, this chapter will focus on the variables that have been retrospectively associated with tibial stress fracture injury history in runners and the effects of fatigue on these variables, both in terms of fatigue-failure mechanics from a materials science perspective and more commonly described global fatigue due to prolonged exercise. Novice female runners have among the highest risk of tibial stress fracture injury among sub-populations of runners, therefore the training and load related factors will be considered in terms of the effects on this population, although in some cases evidence from recreational and well-trained runners will be presented since female runners in general are underrepresented in biomechanics research. Therefore, the purpose of this literature review is to describe the relationship between common training habits and tibial stress fracture injury in endurance running using the traditional research paradigm that attributes high peak loads to injury; a new paradigm of mechanical fatigue that considers how running speed, duration, and volume contribute to injury development; and with a focus on novice female runners, a subpopulation of runners more susceptible to tibial stress fracture injuries.

Novice Female Runners

Running for exercise, recreation, and health benefits has a low barrier to participation, and has increased in popularity in recent decades (Scheerder & Vos, 2011). Middle-aged adults ranked running the 10th most popular sporting activity in 1979, and running ascended to the number one most popular activity by 2009 (Scheerder & Vos, 2011). Sporting activity in general has increased among women from 1969 to 2009; the ratio of women to men who participated in any sport increased from ~30/70 to ~50/50 (Scheerder & Vos, 2011). The participation rates in road races of all distances across the United States reflect the popularity of running, particularly for women. In 2018, there were 18.1 million race registrants, with 5k being the most popular distance, and ~60% of race participants were women (Running USA, 2019). The increased participation in physical activity by women likely has public health benefits, as running is effective in improving outcomes associated with hypertension, hypercholesterolemia, diabetes (Williams, 2008), and osteoarthritis (Williams, 2013). However, running-related pain and injury rates are as high as 64.6% (Reinking et al., 2013), and novice runners are at higher risk of injury compared to runners who ran more frequently or for longer durations (Saragiotto et al., 2014; Taunton et al., 2003; Videbæk et al., 2015).

Many studies have attempted to describe factors that may explain the higher risk of injury in novice runners, including the training factors of mileage, pace, and/or training progression (Ramskov et al., 2018; Taunton et al., 2003), anthropometrics (Buist, Bredeweg, Lemmink, van Mechelen, & Diercks, 2010; Nielsen et al., 2014; Taunton et al., 2003), age (Buist, Bredeweg, Lemmink, van Mechelen, et al., 2010; Taunton et al., 2003), sex (Buist, Bredeweg, Lemmink, van Mechelen, et al., 2010; Kaufman, Brodine, & Shaffer, 2000; Taunton et al., 2003; VanDerWorp et al., 2015; Wentz et al., 2011), running experience (Hespanhol Junior et al., 2012; Malisoux et al., 2015; Reinking et al., 2013), and biomechanical factors (Chan et al., 2018; Maas et al., 2018; Moore, Jones, & Dixon, 2012) with inconsistent results. One difficulty in determining which factors contribute to injury risk is inconsistent definitions of different groups of runners based on experience and/or performance. Some studies defined novice runners as those not involved in any sporting activity at all (Moore, Jones, & Dixon, 2015), those who were active once per week but did no running (de Ruiter, Verdijk, Werker, Zuidema, & de Haan, 2014), or those who were physically active and ran up to two times per week (Slawinski & Billat, 2004) or more than 8 kilometers per week (Chan et al., 2018).

The increased participation of female runners (Scheerder & Vos, 2011) and higher incidence of running-related injuries in female versus male runners (Messier et al., 2018; Taunton et al., 2002) suggests a need to better understand how anatomical factors, running mechanics, and training habits interact in female runners. To identify how the aforementioned factors affect injury incidence in females, it is imperative to study females specifically since it is difficult to generalize results from males, or a mix of males and females, to female runners. In response to this need, sex differences relating to running mechanics have received more attention recently. For example, injury risk in females is often attributed to anatomical differences such as having a wider pelvis or larger Q-angle than men. Women have a 2.3 (Grelsamer, Dubey, & Weinstein, 2005) to 4 degree (Weiss et al., 2013) greater Q-angle than men on average. However, the minimal detectable difference in Q-angle was 3 degrees (Weiss et al., 2013), indicating that measurement errors may lead to erroneous differences. Besides, high Q-angles were not associated with injury risk prospectively (Messier et al., 2018). Regarding pelvis width, the distance between anterior superior iliac spines in women and men were similar (Grelsamer et al., 2005; Schache et al., 2003). These results indicate that something other than differences in anatomical structure may contribute to differences in running mechanics and injury risk between men and women.

Although large structural differences are not present in males and females, there are differences in running mechanics. During running, women had greater peak spinal lateral flexion and axial rotation, 3-D pelvic rotation, and hip frontal plane angles compared to males (Schache et al., 2003). Regression analysis revealed that sex explained a significant proportion of these differences in lumbo-pelvic-hip rotation angles (Schache et al., 2003). In general, female recreational runners also showed greater hip internal rotation and adduction knee abduction, and less rearfoot eversion than male runners (Ferber, Davis, & Williams, 2003; Phinyomark, Hettinga, Osis, & Ferber, 2014; Sakaguchi et al., 2014; Sinclair, Greenhalgh, Edmundson, Brooks, & Hobbs, 2012). Sex-specific prediction models were able to classify competitive vs. recreational runners based only on center of mass acceleration at or above 80% accuracy, but with only ~70% accuracy with all runners combined (Clermont, Benson, Osis, Kobsar, & Ferber, 2019). This indicates that sex and running experience contribute to important differences in running characteristics. Investigations on running injuries should separate women and novices to identify how sex and experience affect mechanics. These mechanical differences may interact with training factors and other runner characteristics to affect injury risk in female runners.

The mechanical differences between sexes in healthy runners may contribute to the different injury rates and types present between men and women. Prospective injury incidence is often higher in women than men (Messier et al., 2018; Taunton et al., 2002). Even when injury incidence is similar, the types of injuries women tend to experience differ. Competitive female runners suffered more ankle injuries, versus male runners who experienced more thigh injuries (Ristolainen, Heinonen, Waller, Kujala, & Kettunen, 2009). Unfortunately, many studies investigating training factors and risk of injury type in recreational runner subgroups consider only runner experience and ignore the effects of sex (Kluitenberg, van Middelkoop, Diercks, & VanDerWorp, 2015; Ramskov et al., 2018; Reinking et al., 2013; Saragiotto et al., 2014; Videbæk et al., 2015) although other studies have identified some sex-specific contributions to injury. Injury incidence was higher in women with greater hip internal rotation and navicular drop (Buist, Bredeweg, Lemmink, van Mechelen, et al., 2010; VanDerWorp et al., 2015), higher age (Buist, Bredeweg, Lemmink, van Mechelen, et al., 2010; Taunton et al., 2003), and infrequent running (~1 day per week) (Taunton et al., 2003). Injury risk was also higher in women with poor aerobic fitness (Wentz et al., 2011) and high body mass index (VanDerWorp et al., 2016, 2015), a particularly relevant factor for those who may be starting a running program to improve fitness and decrease chronic disease symptoms or risk. An important challenge novice runners must overcome is determining an appropriate amount of running. Frequency, intensity, and duration of running are easily modifiable and training errors are commonly attributed to causing running injuries (Hreljac & Ferber, 2006). There are basic principles to consider in any training program regardless of experience level, and many ways to monitor training to balance risk and benefit.

Training Load

Training to improve performance in any sport follows a basic set of principles: specificity, progressive overload, reversibility, and recovery (Powers & Howley, 2001). Generally, these principles explain that you must practice the activity or movements used in performance, training volume and intensity should increase incrementally and at times demand more effort than is comfortable, ceasing training will lead to a decrease in capacity, and body tissues require periods of rest to remodel. In theory, an imbalance in any of these factors will lead to the negative adaptations of overtraining or injury. Running injuries are often attributed to training errors of too much volume, intensity, or progressing volume or intensity too quickly (Hreljac et al., 2000). The incidence of running-related injury in runners of all levels is high (Hespanhol Junior et al., 2013; Kluitenberg et al., 2015), indicating that some imbalance in the application of these basic training principles is common.

Endurance training programs for all levels of runners from novice to competitive prescribe varying volumes and intensities of running and/or walking (Moore et al., 2012; Ramskov et al., 2018; Slawinski, Demarle, Koralsztein, & Billat, 2001; Stoggl et al., 2014). Novice programs begin with modest volume (~15-km) (Ramskov et al., 2018), frequency (3 days/wk) (Ramskov et al., 2018; Taunton et al., 2003), duration (15-35 minutes per session) (Moore et al., 2012; Taunton et al., 2003), and intensity (easy/moderate) (Moore et al., 2012; Ramskov et al., 2018). Advanced training programs may prescribe daily training sessions of short (60 minutes) or long (3 hours) duration, and at intensities ranging from low to high (Stoggl et al., 2014), and programs often use some performance metric to prescribe intensity, such as heart rate (Esteve-Lanao, Foster, Seiler, & Lucia, 2007; Stoggl et al., 2014). Periodically increasing running volume, running intensity, or both, achieves both progression and overload in these training programs, with novice programs progressing more modestly (Esteve-Lanao et al., 2007; Moore et al., 2012; Ramskov et al., 2018; Stoggl et al., 2014; Taunton et al., 2003). Finally, recovery is an important component in a training program that allows the body tissues to remodel and adapt to the demands of training, thus leading to performance improvements. Short duration training programs described for novice runners may not specify a recovery period (Moore et al., 2012), while programs over several weeks or months specify repeated periods of training and recovery (Ramskov et al., 2018; Stoggl et al., 2014). These studies compared how different training programs improved performance outcomes such as maximal oxygen consumption (Moore et al., 2012; Stoggl et al., 2014) or running economy (Moore et al., 2012). If or how the volume and intensity of the different training strategies affect injury outcomes is unknown.

Prospective investigations of runners' training habits do not provide strong support that training factors of high running volume, intensity, or progression are responsible for the high incidence of running-related injuries (Hreljac et al., 2000; Nielsen et al., 2014; Ramskov et al., 2018). Injury incidence is negatively associated with running experience (Hespanhol Junior et al., 2012) and runners who incorporate interval training, and therefore some proportion of high to very high intensity running, have shown lower injury incidence than runners who do not do interval training (Hespanhol Junior et al., 2013). Surveys of training habits also indicate that infrequent running (<2 days/week and < 2 hours/week or less), and therefore relatively low running volumes, increased injury risk in some subpopulations of runners (Malisoux et al., 2015; Saragiotto et al., 2014). These studies on training habits indicate that other factors may have a larger impact on injury outcomes than training factors alone.

Training-related outcomes that incorporate individualized responses to training may elucidate how training factors affect injury risk. Attempts to quantify the "training load" of running use a variety of internal load metrics such as rating of perceived exertion (RPE) (Balsalobre-Fernańdez, Tejero-Gonzaĺez, & Del Campo-Vecino, 2014; Borresen & Lambert, 2008; Wallace, Slattery, & Coutts, 2014) or heart rate response (Balsalobre-Fernańdez et al., 2014; Borresen & Lambert, 2009), combined with external load metrics such as running frequency, intensity, duration, and/or volume (Balsalobre-Fernańdez et al., 2014; Borresen & Lambert, 2009; Eckard, Padua, Hearn, Pexa, & Frank, 2018; Wallace et al., 2014; Wood, Hayter, Rowbottom, & Stewart, 2005). Some wearable sensors also base an estimate of training load on external training factors of distance and speed, called a Training Stress Score, which considers the various speeds used in training (Skiba, 2006; Wallace et al., 2014). This method of monitoring training load was more accurate than RPE and heart rate methods to estimate fitness and fatigue (Wallace et al., 2014). The affordability of these sensors and associated software for analyzing and interpreting the data can range from $100-200 ("RunScribe – The Ultimate Running Analysis Tool," n.d.; "Stryd, Power Meter for Running," n.d.), making them popular in the running community to track progress and improve performance and an important area of clinical biomechanics research (Willy, 2018)

The goal of quantifying training in this manner is to modify training appropriately to improve performance outcomes based on the individualized response of a runner (Gabbett, 2016). Athletes can monitor if or when their training load exceeds their capacity and they require a period of recovery (Gabbett, 2016), An indirect outcome of monitoring load in this manner is the potential to decrease injury risk (Gabbett, 2016), although there is no direct evidence that using these devices is effective for injury prevention. These internal and external load metrics relate to physiological or cognitive response to training intensity and duration, and should not be confused with the biomechanical definitions of internal and external load, e.g. muscle forces and ground reaction forces. However, the effectiveness of the variable speed model to track training load implies that an association between the physiological demand at different intensities and varying mechanical loads experienced by the body exists, and may be a factor in fatigue and injury (Wallace et al., 2014). The mechanical loads experienced by runners at different running speeds, particularly the high magnitude loads with fast running, are often attributed to the development of injuries (Hreljac, 2004). However, as with clinicians concerned with tracking the total training load an athlete experiences, biomechanics researchers are beginning to consider how the range of load magnitudes a runner is experiencing over a volume of training affects the risk of injury due to cumulative effects on anatomical structures (Edwards, 2018). This idea draws heavily on fatigue-failure mechanism concepts from materials science (Edwards, 2018; Gallagher & Schall Jr., 2017).

Injury as a Fatigue-Failure Mechanism

In materials science, fatigue-failure refers to the progressive structural changes (cracks or eventual complete fracture) to a material resulting from stresses and strains applied to a material structure once these forces have been applied a sufficient number of times (Gallagher & Schall Jr., 2017). “Mechanical fatigue” describes fatigue of this nature. This differs from the endurance sports definition of fatigue, which relates to the decline of physical performance and cognitive perception that occurs during prolonged and/or intense physical activity (Enoka & Duchateau, 2016). “Performance fatigability” will refer to the change in performance and perception that occurs during prolonged running. Fatigue-failure concepts in material science describe the relationship between load magnitudes applied to a structure and the number of loading cycles that will lead to failure (Figure 2.1) (Gallagher & Schall Jr., 2017). Any material will experience failure through application of one high-magnitude load, the ultimate stress, or through repeated applications of loads at some percentage of the ultimate stress (Gallagher & Schall Jr., 2017). At lower levels of stress, a higher number of loading cycles may be withstood, and in non-biological materials the endurance limit where an infinite number of loading cycles is possible occurs at ~30% ultimate stress (Gallagher & Schall Jr., 2017), while it is unlikely that an infinite endurance limit exists in biological tissue. Materials may experience a variety of load magnitudes and a varied number of loading cycles at each magnitude, all of which may contribute to fatigue and failure. The cumulative load a material structure experiences from a contribution of varying loads and loading cycles to material damage is often quantified using the Palmgren-Miner rule (Equation 1):

$$c = \sum_{i}^{k} \frac{n_1}{N_1} + \frac{n_2}{N_2} + \cdots \frac{n_k}{N_k} \qquad [1]$$

where c is a constant typically set to equal 1, n_i is the number of cycles applied to the material at a force level with N_i loading cycles to failure (Gallagher & Schall Jr., 2017).

In running, the fatigue-failure concept relates to the common gait retraining strategy of increasing step frequency, an intervention often used to decrease pain or injury risk. Running with a higher step frequency at a given speed decreases peak loads (Hobara, Sato, Sakaguchi, Sato, & Nakazawa, 2012; Wellenkotter, Kernozek, Meardon, & Suchomel, 2014). Studies that showed decreased pain and injury incidence in runners by decreasing peak loads through gait retraining also support the application of fatigue-failure mechanics to running-related injury mechanics (Chan et al., 2018; Noehren, Scholz, & Davis, 2011). The strategies of decreasing step length or the changes required to "run softer" decreases the peak loads applied to a given anatomical structure to a lower percentage of the ultimate stress and allow the structure to withstand a higher number of loading cycles while still remaining below the injury threshold (M. Baggaley, Willy, & Meardon, 2017; Chan et al., 2018). The fatigue-failure relationship of human biological tissues is difficult to determine in vivo for obvious ethical reasons, however animal and computer modeling have provided some useful insight into the response of bone and tendon to repetitive loading.

The relationship between load magnitude and repetitive loading that has been demonstrated or modeled in biological tissue also supports the application of fatigue-failure mechanics to running-related injury (Carter & Caler, 1983, 1985; Fung et al., 2010, 2009). However, as suggested earlier, the ex vivo response of human bone samples to various load magnitudes indicates that bone tissue does not exhibit an endurance limit where it can withstand an infinite number of repetitive loading cycles without experiencing failure. Instead, loading bone cyclically at different strain magnitudes caused failure in approximately 2147 loading cycles (Carter, Caler, Spengler, & Frankel, 1981). However, the hysteresis response of bone showed that a larger strain rate had a greater effect on the bone's ability to recover after each loading cycle towards the end of the fatigue life (Carter et al., 1981). The strain magnitude used experimentally (Carter et al., 1981) was approximately twenty times that measured in human tibia bones during jogging at a slow speed (Lanyon, Hampson, Goodship, & Shah, 1975) and ten times that measured during fast marching (Milgrom et al., 2007). Based on the results of Carter et al. (1981), the tibia bone strain rates measured during running would lead to failure in 100,000 to 1 million loading cycles, equivalent to the loading cycles required to run 100 to 1000 miles. Consequently, the lower range of this mileage estimate is easily achievable within 8 weeks for an individual running 4 times per week and corresponds to the time period during which many running-related stress fractures occur (Burr, 1997), further strengthening the idea of musculoskeletal injury as a fatigue-failure mechanism.

The material properties of biological tissue differ from non-biological materials primarily in that they are not static. Acute negative changes to cellular structure occur due to repetitive loading within an exercise session, stimulating positive long-term adaptations. In bone, exercise associated with high vertical forces (running and jumping) significantly increased bone mineral density in premenopausal women (Vainionpaa et al., 2006). The increase in bone mineral density that occurs due to running and jumping is meaningful, since low bone density is a factor in tibial stress fracture injuries (Franklyn & Oakes, 2018). This adaptive response in biological tissue, and studies on training load and injury, indicate that there may be a "sweet spot" of training volume where injury risk is low (Gabbett, 2016) due to an adequate balance of tissue fatigue/damage and adaptation, since both very low and very high training volumes are associated with injury (Gabbett, 2016; Malisoux et al., 2015; Reinking et al., 2013; Taunton et al., 2003; VanDerWorp et al., 2016). A long-term goal of biomechanics research may be to determine where this "sweet spot" occurs for different individuals and for different sports, and may eventually be possible using new research paradigms that apply fatigue-failure concepts. In addition, there is strong evidence that differences in bone parameters between men and women are due to hormonal factors (Franklyn & Oakes, 2018), highlighting the need to study female populations separately from males.

Recent studies have considered the training and running mechanics factors of running speed, stride length, and running volume on bone stress (Edwards et al., 2009, 2010; Taylor et al., 2004). This methodology predicts the probability of tibial stress fracture considering the fatigue strength of bone, the volume of bone estimated from subject anthropometrics, bone adaptation and repair processes, and bone stresses from experimental data (Edwards et al., 2009, 2010; Taylor et al., 2004). The pattern of injury probability was similar across speed (Edwards et al., 2010), mileage, and stride length (Edwards et al., 2009) in that risk of injury peaked and leveled off after approximately 40 days. However, risk was lower with slower speed (Edwards et al., 2010), lower mileage, and with shorter stride lengths at each mileage (Edwards et al., 2009). These results agree with clinical findings on the timing of stress fracture occurrence (Burr, 1997), the theory that training factors of running "too fast" and "too much" lead to injury (Hreljac, 2004), and that gait retraining interventions such as decreasing step length may decrease injury risk (Hafer, Brown, DeMille, Hillstrom, & Garber, 2015), possibly due to the interaction of peak loads and the number of loading cycles as described previously. While running mechanics research has generally focused on peak loads under varying running conditions, new research quantifying the total loads applied over a volume of running are considering this interaction between load and loading cycles.

Cumulative Load

Numerous investigations of the mechanical loads of running have focused on the peak loads applied to the body under various conditions. Peak values of kinetic variables such as ground reaction forces and joint moments typically increase as running speed increases (Brughelli, Cronin, & Chaouachi, 2011; Hamill, Bates, Knutzen, Sawhill, 1983; Novacheck, 1998; Ueda et al., 2016), however a clear association between high peaks loads from fast running and injury history has been inconsistent in retrospective studies (Davis et al., 2016; Kuhman, Paquette, Peel, & Melcher, 2016; Zadpoor & Nikooyan, 2011). Prospectively, gait retraining to decrease peak vertical GRFs during running decreased injury incidence (Chan et al., 2018). In runners experiencing pain due to running-related injury, gait retraining to affect hip kinematics also decreased vertical instantaneous loading rate (VILR), and caused a complete cessation of pain (Noehren et al., 2011). Together, these results indicate that peak loads may have some association with running related injury, but simply measuring peak loads to explain injury risk is insufficient; many runners experience high peak loads per step without developing major injuries. While the peak loads of fast running are higher than slow running within an individual, the proportion of fast to slow running is generally small; from

6-50% in common training strategies (Stoggl et al., 2014). The application of fatigue-failure concepts are an emerging research paradigm that describes how the interaction between peak loads runners experience during various running speeds used in training and the contribution of these speeds to the overall training volume may contribute to the development of running injuries and to furthering our understanding of how to monitor and reduce injury risk.

Recent studies of running-related injury have applied fatigue-failure concepts from materials science to biomechanical studies by calculating cumulative load of locomotion. These estimates represent the total load accumulated by the body or body tissues, and combine information about commonly measured peak loads during locomotion at different speeds, an indication of intensity, with the distance traveled. When locomotion speed increases, there are concomitant increases in peak loads and step length (Hamill, Bates, Knutzen, Sawhill, 1983; Petersen et al., 2015). Changes in these outcome variables will affect the total load accumulated as individuals travel a distance, and cumulative loads may not necessarily be proportional to either the change in load or step length.

Studies quantifying cumulative load in running have use a standardized period of time (Miller, Brent Edwards, & Deluzio, 2015) or distance (Baggaley & Edwards, 2017; Firminger & Edwards, 2016a; Miller, Edwards, Brandon, Morton, & Deluzio, 2014; Petersen et al., 2015). Estimates of knee joint loading during standing, walking, and running for equal amounts of time showed that the load accumulated by the knee during standing and walking were similar, while loads during running were significantly higher (Miller et al., 2015). The higher peak forces during running combined with the higher number of loading cycles that result from higher step frequency during running vs. walking likely contributed to the differences in cumulative load at the different locomotion speeds (Miller et al., 2015). When accounting for differences in stride length, a comparison of knee impulse during walking vs. running found no difference in the per-unit distance load although the peak loads were lower in walking vs. running (Miller et al., 2014). Changing running speed or running technique within individuals has an effect on the load accumulated per kilometer. Subjects running at 8, 12, and 16 kilometers per hour showed similar knee impulse magnitudes at all speeds, however cumulative impulse was significantly greater at the slow speed compared to the fast speed (Petersen et al., 2015).

Commonly manipulated training factors of footwear selection and stride length also have an effect on cumulative load. Switching from a traditional running shoe to a minimalist shoe increased per-step ankle angular impulse and cumulative impulse over an estimated 5-kilometer distance, however cumulative knee impulse decreased (Firminger & Edwards, 2016b). Decreasing stride length at a constant speed increased cumulative ankle impulse, but decreased cumulative knee impulse (Firminger & Edwards, 2016b). When comparing gait retraining strategies, encouraging runners to run softer and switching from a rearfoot to forefoot strike both caused an increase in eccentric and concentric knee and ankle joint work per kilometer compared to baseline, and shortening step length also increased concentric and eccentric work per kilometer at the knee (Baggaley et al., 2017). Together, these studies on cumulative load in running suggest several important points. First, cumulative load may be sensitive to either step length (Lo et al., 2015) or peak load (Baggaley et al., 2017). Second, modifying step length or foot strike pattern (Baggaley et al., 2017), either intentionally or as a result of performance fatigability, may change the loads accumulated throughout the duration of a run under real-life conditions. Finally, thus far estimates of cumulative load do not account for the potential effects of prolonged running on running mechanics or mechanical behavior of biological structures.

The impetus for investigations into cumulative loads during standing, walking, or running is often to explain how load-related overuse injuries develop, whether from constant loading (osteoarthritis) or repetitive loading (running-related injuries). However, there is currently no association between higher or lower cumulative loads with injury development or prevention. Based on the traditional research paradigm that high loads are injurious (Chan et al., 2018; VanDerWorp et al., 2016) it is possible to conclude that accumulating high loads also increases injury risk. However, in most of the cumulative load studies comparing a standardized distance, higher cumulative loads results from slower running where peak loads are low and the number of loading cycles to cover a given distance is high (Petersen et al., 2015). Based on fatigue-failure mechanics, lower loads (stresses) applied to a material allow for an exponentially higher, or even infinite, number of loading cycles before failure occurs (Gallagher & Heberger, 2013; Gallagher & Schall Jr., 2017), which would decrease the risk of injury. However, with repetitive loading the S-N curve of biological tissue will likely shift down as mechanical and morphological changes occur in response to a high number of loading cycles. Measuring how step length, ground reaction force characteristics, and joint loading changes throughout a prolonged run may also reveal how running fatigue affects injury risk.

Tibial Stress Fracture Injury

Running injury rates in endurance runners are high, ranging from 15.6 to 65.6% (Kluitenberg et al., 2015; Malisoux et al., 2015; Napier, MacLean, Maurer, Taunton, & Hunt, 2018; Nielsen et al., 2014). Stress fractures accounted for 6.4 to 21% of all reported running injuries (Battaloglu, 2011; Hespanhol Junior et al., 2012; Kluitenberg et al., 2015), and tibial and metatarsal stress fractures account for 75% of all stress fractures (Battaloglu, 2011). These injuries are arguably one of the more serious running related injuries. Depending on severity, recovery may require complete cessation of activity, medical treatment (physical therapy or surgery), and long healing times, along with slow reintroduction to activity (Warden, Davis, & Fredericson, 2014).

Injury rates in subpopulations of runners differ, showing that new and infrequent runners are at higher risk of injury. Predictive statistical modeling of tibial stress fracture injury probability indicates that injury risk is highest between 1 to 2 months of beginning a new sport activity (Taylor & Kuiper, 2001). Prospective studies and retrospective surveys on training habits and injuries support this finding: novice runners had more than twice the injury incidence than recreational runners per 1000 hours of running (Videbæk et al., 2015), and runners with a training frequency of twice per week or volume of less than two hours per week had higher incidence of injury compared to those who ran more frequently or for a longer duration (Malisoux et al., 2015; Saragiotto et al., 2014; Taunton et al., 2003).

Females also show greater stress fracture injury risk than males. Female athletes have 10 times the relative risk of developing a stress fracture compared to the general population, and running is the highest risk sport for this injury (Battaloglu, 2011). In military recruits, women experience higher injury rates than men, and poor aerobic fitness was one of the factors attributed to injury development (Wentz et al., 2011), providing further support to the idea that risk is greatest at the beginning of a training program.

There are many proposed factors that contribute to the higher risk of injury in female novice runners, including sex differences in bone morphology and density, body composition, and hormonal factors (Warden et al., 2014; Wentz et al., 2011). Biomechanical studies of running injuries often focus on peak loads during running and anatomical factors to explain injury risk or injury development (Bennell et al., 2004; Meardon, Willson, Gries, Kernozek, & Derrick, 2015; Milner, Ferber, et al., 2006). More recently, studies have considered training habits in addition to biomechanical and anatomical factors to determine if the interaction of these factors contributes to injury (Bertelsen et al., 2017; Hreljac, 2004; Hreljac & Ferber, 2006; Paquette & Miller, 2018). This proposed project will investigate primarily how training habits contribute to the cumulative load of variables associated with tibial stress fracture injury risk, and if running fatigue affects the cumulative load and tibial stress fracture risk in novice female runners. This investigation will focus on variables that are associated with tibial stress fracture injury history, namely the VALR, free moment of the vertical GRF, axial tibial bone load, and peak tibial impact acceleration (Milner, Davis, & Hamill, 2006; Milner, Hamill, & Davis, 2007; Pohl, Mullineaux, Milner, Hamill, & Davis, 2008).

Vertical Average Loading Rate

Vertical ground reaction force magnitudes increase concomitantly with locomotion speed within individuals (Hamill, Bates, Knutzen, Sawhill, 1983; Keller et al., 1996; Munro, Miller, & Fuglevand, 1987; Nigg, Bahlsen, Leuthi, & Stokes, 1987). Impact peaks and active peaks increased with speed from slow walking to very fast running in male and female recreational athletes (Keller et al., 1996) and at a range of running speeds in competitive male runners (Hamill, Bates, Knutzen, Sawhill, 1983; Nigg et al., 1987). In addition, the rate of loading also increased with speed in recreational and competitive male runners (Hamill, Bates, Knutzen, Sawhill, 1983; Munro et al., 1987). Ground reaction forces contribute to the loads applied to the tibia during the stance phase in running (Sasimontonkul, Bay, & Pavol, 2007), and peak loads and loading rates are a factor in failure of bone (Pal, 2014), therefore these increased forces and loading rates at higher speeds are often considered a contributing factor to running injuries in general (Davis et al., 2016), and tibial stress fracture injuries specifically (Davis et al., 2004).

The vertical ground reaction force characteristic that has been most consistently associated with running overuse injuries in general is the VALR (Davis et al., 2016; Hreljac et al., 2000; VanDerWorp et al., 2016). VALR is higher in runners with tibial stress fracture injury history in retrospective studies (Milner, Ferber, et al., 2006; Pohl et al., 2008; Zadpoor & Nikooyan, 2011), and was higher in prospective studies in those who went on to developed an injury compared to those who did not (Davis et al., 2004; Davis et al., 2016). Over a two year period, tibial stress fractures were the third most common injury runners experienced and accounted for ~14% of all injuries (Davis et al., 2016). Out of a range of training, anatomical, and biomechanical factors tested in runners with a history of lower leg injury, including multiple and/or bilateral injuries, only vertical loading rates were different when compared to a group of runners who never experienced injury (Hreljac et al., 2000). While the characteristics of the GRFs are an important factor in running mechanics and running injuries, the skeleton also experiences loads applied by muscle contractions.

Compressive Tibial Load

Many studies on the loads experienced by the body focus primarily on ground reaction force characteristics, but overlook the internal forces applied to the bones through muscle contraction. Including internal forces provides a more complete description of the loads applied to the skeleton during running. While peak ground reaction forces during the contact phase of running may reach 2-3 times body weight, estimates of Achilles tendon forces applied to the tibia reach 6 times body weight or higher (Matijevich, Branscombe, Scott, & Zelik, 2019; Sasimontonkul et al., 2007; Scott & Winter, 1990), causing the total compressive load on the tibia to easily reach over 10 times body weight with fast running (Scott & Winter, 1990). However, high vertical GRFs do not necessarily lead to high peak compressive tibial loads: over a range of speeds and inclines, peak compressive load on the tibia was moderately correlated with peak vertical GRFs on average, but negatively correlated with impact peak and VALR (Matijevich et al., 2019). Switching from a rearfoot strike to forefoot strike pattern decreased peak VALR and VILR but not peak tibial strain or estimated probability of stress fracture injury (Chen et al., 2016). This is likely because peak Achilles tendon loads are slightly higher with a forefoot strike (~0.5 BW), which also led to significantly greater Achilles tendon cumulative loads (Almonroeder, Willson, & Kernozek, 2013). Understanding how different training factors such as running speed, duration, and total volume contribute to the combined external and internal loads that constitute the total compressive force on the tibia will fill an important gap in understanding how these factors affect tibial stress fracture injury risk.

Free Moment

The free moment of the ground reaction force, which quantifies the frictional forces between the plantar surface of the foot on the ground, is often used as a surrogate measure of torsional loading on the tibia bone. Runners with tibial stress fracture injury history demonstrate higher free moment magnitudes compared to age and mileage matched controls (Milner, Davis, et al., 2006; Pohl et al., 2008). Binary logistic regression, used to determines if an outcome variable may predict the odds of being a case, determined that free moment magnitudes alone predicted tibial stress fracture injury group membership in 66% of cases (Milner, Davis, et al., 2006), and 83% of cases when combined with hip adduction and rearfoot eversion (Pohl et al., 2008). In addition, logistical modeling indicated that the likelihood of having tibial stress fracture injury history increased 1.365 times for every 0.001 Nm/BW*Ht increment increase in free moment (Milner, Davis, et al., 2006). To date, there are no known prospective studies linking free moment magnitudes to stress fracture injury development, so whether large free moments are a cause or result of tibial stress fractures is unknown. However, the strong association with tibial stress fracture injury history and sensitivity of injury risk to increases in free moment (Milner, Davis, et al., 2006) make it an important variable to consider in tibial stress fracture injury studies.

Tibial Impact Acceleration

Retrospectively, tibial impact acceleration is higher in runners with a history of tibial stress fracture compared to runners who have never experienced a tibial stress fracture (Milner, Ferber, et al., 2006; Milner et al., 2007), and was higher in a small group of female runners who went on to develop a stress fracture prospectively (Davis et al., 2004). Gait retraining strategies directing runners to “run softer” (Creaby & Franettovich-Smith, 2016) and providing visual and/or auditory feedback on impact acceleration magnitudes during running effectively cause a substantial decrease in tibial impact acceleration (Clansey, Hanlon, Wallace, Nevill, & Lake, 2014; Creaby & Franettovich-Smith, 2016), Providing quantitative real-time feedback from an accelerometer and following verbal cues from a clinician were equally successful in decreasing impact acceleration (Creaby & Franettovich-Smith, 2016). Tibial impact acceleration correlated strongly with loading rate of the GRF

(Hennig, Milani, & Lafortune, 2016). Commercially available wearable devices use accelerometer technology to measure running metrics and provide feedback to the user. These devices are affordable (~$30), easy to use, and provide easily understood information that allow athletes or clinicians to make inferences about difficult to measure metrics such as loading rate (Hennig et al., 2016; Willy, 2018). The ease with which runners can manipulate impact acceleration, and therefore likely ground reaction force characteristics, through simple gait retraining strategies make impact acceleration an attractive metric to runners interested in preventing injury (Willy, 2018). Impact acceleration is also sensitive to performance fatigability in running, discussed in greater detail in the subsequent section.

Performance Fatigability

A main limitation in describing the effects of performance fatigability in running is the lack of consensus on a definition of fatigue, and the varying and inconsistent experimental definitions that result. For example, fatigue was defined as a decline in central nervous system input (central fatigue), muscle performance (peripheral or neuromuscular fatigue) (Froyd, Beltrami, Millet, & Noakes, 2016), a change in physiological outcomes (Mizrahi, Verbitsky, & Isakov, 2000; Oyono-Enguelle et al., 1990), or increased rating of perceived exertion (RPE) due to the discomfort or pain associated with prolonged exercise (Baron et al., 2008; Boulay, Simoneau, Lortie, & Bouchard, 1997). Enoka & Duchateau argue that the multifactorial nature of fatigue does not lend itself to typical reductionist scientific techniques, and instead investigations should consider changes in both performance fatigability (blood flow, metabolic byproducts, muscle activation) and perceived fatigability (arousal, pain) (2016). They suggest that performance fatigability studies follow the framework of selecting some performance outcome, such as time to failure, then consider the additional fatigue-related adjustments to outcomes such as rate of change of force, RPE, and heart rate (HR) that limit this particular outcome (Enoka & Duchateau, 2016). According to this proposed framework, the performance outcome of this research is the distance traveled, and the factors that contribute to performance fatigability of this outcome are the biomechanical variables associated with tibial stress fracture injury (VALR, free moment, tibial load, tibial impact acceleration), physiological outcomes (blood lactate accumulation and HR), and cognitive factors (RPE).

Performance Fatigability and Running Mechanics

Decreases in muscle power production and activation that occur after many contraction cycles cause changes in running mechanics. In competitive male runners, performing maximal countermovement jumps for 60 seconds caused decreased step length, step frequency, flight time, loading rate, and peak vertical ground reaction forces (Fischer et al., 2015). Thirty minutes of supra-ventilatory threshold running caused an increase in activation of the gastrocnemius muscle with a corresponding decrease in activation of the tibialis anterior muscle in recreational male runners (Mizrahi et al., 2000). Prolonged running caused a similar effect in animal models, where quadriceps activation increased and hamstring activation decreased with prolonged running in dogs (Yoshikawa et al., 1994). Together, these studies indicate that muscle activation patterns and muscle force production changes after prolonged running, there may be an imbalance in muscle activation and muscle force production between anterior and posterior leg muscles, and this imbalance may lead to an imbalance in the load applied to passive structures, i.e. bones (Mizrahi et al., 2000).

The muscle activation and force production changes that occur during prolonged exercise may lead to changes in movement patterns that affect the joint kinematics and kinetics in running. In particular, the variables associated with tibial stress fracture show some sensitivity to prolonged running, and temporospatial changes often occur, although the experience and fitness of the runner may have an effect. Untrained runners showed an increase in cadence and decrease in step length in response to a fatiguing protocol that required participants to reach volitional failure, qualified by an RPE rating of 19/20 (Willson & Kernozek, 1999). In healthy males, 15 minutes of supra-ventilatory threshold running caused stride rate to decrease and tibial impact acceleration to increase compared to the beginning of the run, both of which persisted until the end of 30 minutes of running (Mizrahi et al., 2000; Verbitsky, Mizrahi, Voloshin, Treiger, & Isakov, 1998). When running to exhaustion, defined by an RPE of 17/20, novice runners lasted longer than competitive runners (28 vs 15 min) but neither group showed changes in temporospatial parameters (Maas et al., 2018). In a group of healthy but untrained males, those who exhibited a decrease in end-tidal pressure of carbon dioxide (a physiological variable indicating performance fatigability) while running at ventilatory threshold showed increased tibial impact acceleration after 5 minutes of running, and decreased stride rate after 15 minutes of running, while those who maintained constant end-tidal pressure of carbon dioxide showed no changes in tibial impact acceleration or stride rate (Verbitsky et al., 1998).

Highly trained and competitive runners seem to maintain movement patterns over typical durations of running better than less fit runners, but occasionally show similar changes in tibial impact acceleration. In competitive runners, running for approximately 18 minutes at ventilatory threshold had no effect on kinematics, tibial impact acceleration, or shock attenuation (Abt, John et al., 2011). After completing a long run of approximately 90 minutes, well-trained male runners showed an increase in loading rate of the GRF, but no change in rearfoot or hip kinematics (Paquette & Melcher, 2017). Trained male runners running at the speed associated with the onset of blood lactate accumulation steadily increased RPE rating over 2 20-minute bouts of running (Clansey et al., 2016). Stride length, stride rate, and tibial impact acceleration showed no change throughout the run (Clansey, Hanlon, Wallace, & Lake, 2012; Clansey et al., 2016), but ground reaction force characteristics showed higher free moment and VALR after only 20 minutes of running, and VALR increased further after an addition 20 minutes (Clansey et al., 2012). During a 5k time trial, trained runners showed a 6.7% increase in tibial acceleration by the middle of the run that increased to 20.7% by the end (Derrick, Dereu, & Mclean, 2002). Conversely, well-trained female runners showed a decrease in loading rate and increase in step length after completing a fatiguing protocol (Gerlach et al., 2005).

It appears that the level of experience and fitness of a runner may affect the degree to which they experience performance fatigability. In addition, the relationship between various metrics used to quantify fatigability, i.e. HR, blood lactate, RPE, and modifications to running mechanics are unknown. No running biomechanics studies include details on performance fatigability of running mechanics outcomes associated with tibial stress fracture in association with fatigability of physiological and perceptual factors. The inconsistency of performance fatigability of running mechanics suggests that a combination of running duration and/or intensity may be required to elicit mechanical changes (Abt et al., 2011; Derrick et al., 2002; Gerlach et al., 2005; Paquette & Melcher, 2017), and running experience will affect what that duration and intensity should be (Clansey et al., 2016; Maas et al., 2018; Verbitsky et al., 1998). In addition, limited research on female runners specifically indicates that women may respond to prolonged running differently from men (Gerlach et al., 2005), but most performance fatigability studies investigating stress fracture risk variables use well-trained or active males (Abt et al., 2011; Clansey et al., 2016; Derrick et al., 2002; Mizrahi et al., 2000; Mizrahi, Verbitsky, Isakov, & Daily, 2000; Paquette & Melcher, 2017; Verbitsky et al., 1998), or a mix of males and females (Maas et al., 2018). How prolonged running affects the modification of variables associated with tibial stress fracture injury in novice female runners throughout a run is unknown. Understanding if or how female novice runners modify gait in response to prolonged running, and how these modifications affect variables associated with tibial stress fracture injury may allow coaches to improve training recommendations for this population and mitigate injury risk.

Performance Fatigability and Physiological Factors

The changes in physiological factors of HR and blood lactate concentration over prolonged periods of exercise may contribute to performance fatigability of prolonged running. Cycle ergometry is a preferred activity for performance fatigability studies due to the ability to control and measure exercise intensity. Well-trained males cycling for 90 minutes at the heart rate associated with ventilatory threshold, 71.3% of maximal oxygen consumption (VO_2 max) on average, were able to maintain a consistent heart rate only with a gradual decrease in work output (Boulay et al., 1997). When well-trained males cycled at a consistent workload associated with the lactate steady-state, between 73-83% VO_2 max, they were able to cycle for 55 minutes on average, and HR gradually increased from 151 to 175 beats per minute (Baron et al., 2008). HR also increased gradually during steady-state cycling exercise at 66, 73.2, and 80.8% of VO_2 max in well-trained male runners (Oyono-Enguelle et al., 1990). The magnitudes of HR were higher at the higher vs. lower intensities in the early stages and end of the exercise bout, though the magnitudes of the change were similar

(Oyono-Enguelle et al., 1990). The duration of the exercise was also different, participants were stopped after 45 minutes at the lowest intensity, and time to exhaustion at 73.2 and 80.8% of VO_2 max was 42.1 and 23.5 minutes, respectively (Oyono-Enguelle et al., 1990). Similar results were also seen in well-trained male and female cyclists whose HRs steadily increased during steady state cycling for 30, 60, and 90 minutes at 90% anaerobic threshold power (Foster et al., 2001a). It appears that regardless of exercise intensity, HR increases throughout steady state exercise, while the intensity dictates only the magnitude of the HR response and to a smaller degree the magnitude of the increase.

The aforementioned studies also measured blood lactate response to the steady-state exercise. When workload was gradually decreased to maintain a constant HR, blood lactate accumulation decreased according to the workload (Boulay et al., 1997). Prolonged cycling at the intensity associated with the lactate steady-state showed that lactate accumulation decreased significantly by the end of exercise after the initial increase that commonly occurs during the first ~20 minutes of exercise (Baron et al., 2008). When comparing a range of exercise intensities, blood lactate accumulation at the lowest exercise intensity (66% VO_2 max) increased similarly at the onset of exercise compared to higher exercise intensities (73.2 and 80.8% of VO_2 max). However, blood lactate accumulation gradually decreased towards the end of exercise at the lowest intensity, while at the two higher intensities it continued to increase until termination of exercise (Oyono-Enguelle et al., 1990). Blood lactate accumulation differs in HR response such that at lower exercise intensities it may not be a large contributor to performance fatigability, since blood lactate accumulation decreases after the initial increase that occurs at the onset of exercise, while HR gradually increases throughout regardless of intensity. These studies tested well-trained subjects, and while untrained subjects likely have a similar HR and lactate response to steady-state exercise, no similar studies on untrained subjects were found. It is unknown if HR response or blood lactate accumulation contribute to performance fatigability in novice female runners during a prolonged run to volitional failure. This gap in knowledge is important because identifying a relationship between easy to measure metrics such as HR and blood lactate accumulation, and difficult to measure metrics such as the VALR, free moment, and tibial axial load, may improve the ability of commercially available wearable devices to extrapolate load-related information that contributes to injury risk.

Performance Fatigability and Perception

RPE is an overall indicator of physical strain that incorporates various factors contributing to that strain, i.e. sensations from muscles and joints, heart rate, and depth and rate of breath (Borg, 1982). The 6-20 scale developed by Borg has shown high correlation with heart rate and other physiological variables (Borg, 1974) and therefore is commonly used to measure subjective exercise intensity and feelings of fatigue. Some studies that investigated performance fatigability in running measured RPE during exercise, but it was primarily used as termination criteria rather than an outcome variable (Clansey, Lake, Wallace, Feehally, & Hanlon, 2016; Dierks, Davis, & Hamill, 2010; Maas et al., 2018; Willson & Kernozek, 1999). However, since these studies chose to terminate exercise once RPE reached a predetermined threshold, it implies an expectation that the perception of fatigue would increase throughout a run, and may indicate the point at which other fatigability outcomes (i.e., running mechanics) would also change (Dierks et al., 2010; Maas et al., 2018; Willson & Kernozek, 1999). Cycle ergometry is more commonly used when quantifying the effects of exercise duration or intensity on RPE due to greater control on exercise intensity via power meters. Cycling at maximal lactate steady state for 55 minutes resulted in a constant RPE of 3/10 until the end of exercise when RPE increased to 6/10 (Baron et al., 2008). RPE increased concomitantly with HR, from an RPE of 0/10 at rest to 3.8/10, 4.3/10, and 4.9/10 during steady-state cycling at 90% anaerobic threshold for 30, 60, and 90 minutes, respectively (Foster et al., 2001a). These results indicate that RPE is sensitive to exercise intensity and duration, and useful to quantify perception of exercise intensity and performance fatigability in running and cycling. However any association between RPE, performance fatigability of running, and running mechanics is unknown. RPE is also a popular metric used to estimate training load (Borresen & Lambert, 2009; Foster et al., 2001a; Seiler & Kjerland, 2006; Wallace et al., 2014). If a relationship between RPE and GRF characteristics exist, it could improve the ability of runners and coaches to assess injury risk based on training time and perceived intensity.

Summary

The theoretical basis that a combination of training factors (speed, volume, progression) and the training load contribute to running related injuries is strong. In practice defining training load from a "coaching" perspective using methods such as training impulse or session RPE, which consider exercise time and heart rate or perceived difficulty, or from a biomechanical perspective measuring the loads from GRF or muscle contraction, demonstrates this basis. However, the appropriate combination of training volume and intensity that runners of all levels may perform without leading to injury is unknown, which limits the development of best practices for minimizing injury risk. The effects of fatigue on novice female runners, specifically on the cumulative loading of variables associated with tibial stress fracture injury risk for which this population show greater risk, are largely unknown. Describing how prolonged running affects these variables in this population may eventually lead to improved training recommendations and decreased injury risk. Specific unanswered questions that could clarify how training factors affect the cumulative loading of tibial stress fracture injury variables during running, and whether the cumulative load is associated with injury risk are:

1. How does running at different speeds over a volume of training affect the cumulative load of variables associated with tibial stress fracture injury history in runners with a range of running experience?
2. How does performance fatigability of running during a single, prolonged run affect the peak and cumulative loads of variables associated with tibial stress fracture injury in novice female runners? In addition, is there any association between the effects of performance fatigability on peak/cumulative loads, physiological response, or perception quantified by blood lactate accumulation, HR and RPE?
3. Do the effects of performance fatigability on axial tibial load affect the tibial stress fracture injury probability in novice female runners?

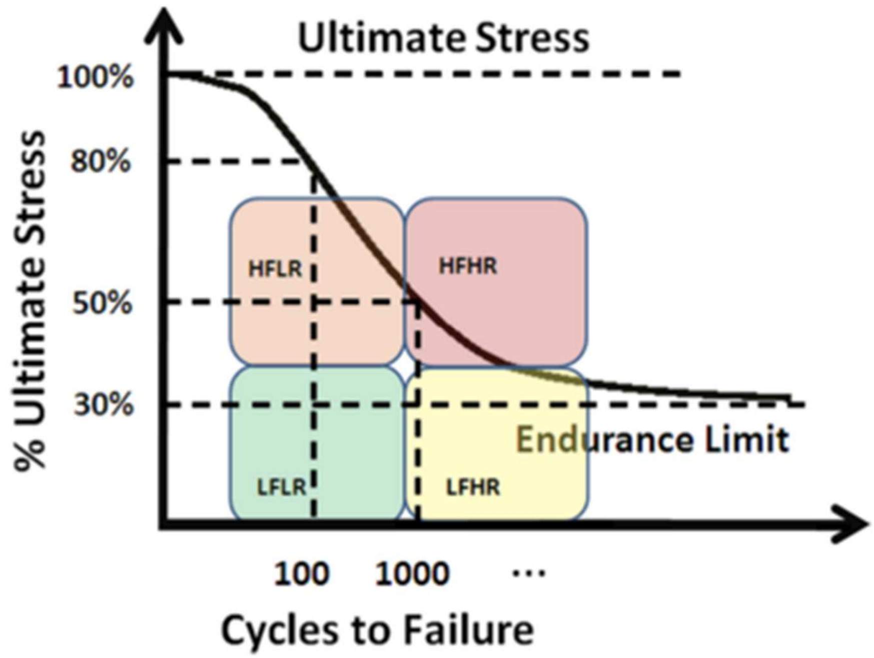

Figure 2.1. The S-N relationship to 4 loading conditions: LFLR: low force-low repetitions, LFHR: low force-high repetitions, HFLR: high force-low repetitions, HFHR: high force-high repetitions. (Gallagher & Schall, 2017)

Chapter 3: Fast running does not contribute more to cumulative load than slow running

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Introduction

Training programs for general health and performance often prescribe varying proportions of exercise intensity depending on outcome goals (Moore et al., 2012; Morris et al., 2017; Slawinski et al., 2001; Stöggl & Sperlich, 2014). While the volumes and proportions of high versus low intensity running or walking may vary based on fitness level and training goal, incorporating proportions of each may be beneficial for runners with a range of fitness and experience (Hespanhol Junior et al., 2013; Moore et al., 2012; Morris et al., 2017; Slawinski et al., 2001; Stöggl & Sperlich, 2014). Running injury incidence has been found to be between 16-31% (Chan et al., 2018; Hespanhol Junior et al., 2013). The etiology of most running-related injuries is still not well understood and injury development is often attributed in whole or in part to so-called "training errors" such as too much volume, too much intensity, or progressing volume and or intensity too quickly (Lysholm & Wiklander, 1987; Ramskov et al., 2018), as well as to biomechanical factors such as impact forces and internal loading (Edwards et al., 2009; Hreljac, 2004).

Previous studies on intensity of training have reported that interval training, typically performed at a relatively fast speed, is associated with a lower rate of injury in recreational runners (Hespanhol Junior et al., 2013; van Poppel, de Koning, Verhagen, & Scholten-Peeters, 2016), suggesting that running at different proportions of speeds in a set training volume may be beneficial for injury prevention. The peak values per stride of most load-related variables in running increase with increasing speed (Hamill, Bates, Knutzen, Sawhill, 1983; Novacheck, 1998), while the rate of "cumulative loading", typically computed as the ratio between a load-related variable and the stride length, appears to decrease with increasing speed (Miller et al., 2014; Petersen et al., 2015). Assessments of cumulative loads in running have been popular recently in studies on running-related injuries (Baggaley & Edwards, 2017; Miller et al., 2014; Petersen et al., 2015) and running injuries in general can be theoretically modeled as mechanical fatigue phenomena, where the damage accumulated by a structure from mechanical loading over time outpaces the structure's ability to repair/recover/remodel (Edwards, 2018). However, it is currently unknown how different proportions of fast or slow running speed within a given volume of training affects the loads applied to and accumulated by the body. This gap in knowledge is important for clarifying the role of speed distributions during training on cumulative loads, which is a necessary precursor to a better mechanistic understanding of how cumulative load (or load in general) affects running injury.

Several retrospective and prospective studies have shown that ground reaction force (GRF) characteristics and the vertical loading rate in particular may be associated with running injuries in general, and with tibial stress fracture specifically (Chan et al., 2018; Davis et al., 2016; Hreljac et al., 2000; Milner, Ferber, et al., 2006; Napier et al., 2018; Pohl et al., 2008). The vertical GRF makes a relatively small contribution to tibial loading during running while force applied to the tibia via the Achilles tendon accounts for up to 80% of the peak compressive tibial load in running (Sasimontonkul et al., 2007) which can reach 13 times body weight at fast running speeds (Burdett, 1982; Sasimontonkul et al., 2007; Scott & Winter, 1990). The relationship between peak load and cycles to failure in bone is highly nonlinear (Carter & Caler, 1983, 1985) so even small differences in peak tibial loads such as those sustained during different speed combinations used in training may also affect likelihood of tibial stress fracture injury. Along with vertical loading rate and tibial loads, there is also evidence that external torsional loading contributes to the development of stress fractures. Specifically, the free moment of the GRF was greater in runners with a history of tibial stress fracture compared to controls, and predictive of membership in the tibial stress fracture group (Milner, Davis, et al., 2006; Pohl et al., 2008). Loading rates, muscle forces, and free moments increase concomitantly with speed (Hamill, Bates, Knutzen, Sawhill, 1983), and exposure to higher peak values of these load-related variables may be associated with injury (Milner, Davis, et al., 2006; Milner, Ferber, et al., 2006). However, it is currently unknown if or how running speed affects the accumulation of variables associated with stress fracture when different combinations of speed are used within a given volume of training.

Therefore, the purpose of this study was to compare the vertical average loading rate (VALR), peak free moment, and peak axial tibial load between two different proportions of running speed over an equal distance: (i) all distance at a "normal" self-selected speed, and (ii) the same distance split between self-selected "slow" and "fast" speeds such that the average speed equaled "normal". Per-step magnitudes of each load variable and step length were expected to increase concomitantly with speed. It is unclear if load peaks or step lengths are more sensitive to speed, therefore we hypothesized that running all distance at normal speed and running the same distance at the same average speed using a combination of slow and fast speed would have similar estimated cumulative VALR, free moment, and tibial load, and that the slow and fast speed would contribute similarly to the total cumulative load of the slow and fast combination.

Methods

Participants

Previous studies on free moment and VALR in injured and uninjured runners have used sample sizes of 40-50 to achieve desired error rates of $\alpha = 0.05$, $\beta = 0.20$, and reported effect sizes of 0.56-0.99 (Milner, Davis, et al., 2006; Milner, Ferber, et al., 2006). Recreational runners from the local community were recruited to participate via contact with local running and endurance sports clubs. Inclusion criteria were (i) age between 18-50 years, (ii) run at least three times per week on average and train for at least one race per year, and (iii) have had no lower limb surgeries in the past year and no major health issues in the past year that have affected their ability to walk, run, or exercise for more than a week consecutively. Protocol approval was obtained from the University of Maryland Institutional Review Board. A total of 43 participants (29 female and 14 male, 24 ± 6 yr, 1.68 ± 0.10 m, 63.12 ± 9.61 kg) completed this study. Participants represented a wide range of skill with an average weekly mileage of 25 mi (range: 6-70 mi), and all were habitually shod runners. Each participant gave written informed consent and completed a questionnaire on their exercise and injury history. The minimum detectable effect size with $\alpha = 0.05$, $\beta = 0.20$, was 0.43 in a paired Student's *t*-test.

Experimental Setup

Participants wore their own running shoes and form-fitting spandex shorts. Participants wore 33 reflective markers on the pelvis (iliac crests, anterior superior iliac spines, posterior superior iliac spines, sacrum), lower extremity of the dominant leg, defined as the leg used to kick a soccer ball (greater trochanter, four-marker thigh cluster, lateral and medial epicondyles, fibula, shank, lateral and medial malleoli), and both feet (great toe, first and fifth metatarsal, calcaneus) (Krupenevich, Pruziner, & Miller, 2017). Marker positions were captured using a 13-camera motion capture system (VICON, Centennial, CO, USA) sampling at 200 Hz. Eight embedded force plates (Kistler, Amherst, NY, USA) measured GRF at 1000 Hz. The motion capture space is defined by the consecutive placement of the force plates on a 12-m straight stretch of the track. Participants first performed a static calibration trial by standing still with their feet shoulder-width apart and shoulders abducted to ~90 degrees for 10 seconds.

For movement trials, calibration markers were removed and participants ran around a 50-m indoor track for three laps each at three speeds (nine laps total): self-selected “slow”, “normal”, and “fast” speeds. Specifically, participants were instructed to run at a recovery/conversation pace for slow speed, a moderate pace for normal speed, and a tempo or 5k race pace for fast speed and ran freely based on these instructions. The “fast” speed was therefore likely substantially slower than each runner’s “maximum” speed, i.e. an all out-sprint. However, many interval training programs and workouts prescribe paces at or near the target race pace in long-distance running. Participants were cued to change speed upon completion of the third pass through the motion capture space at the previous speed, allowing for at least 30 meters to accommodate to the new speed.

Data Reduction

Data processing was performed using Visual3D software (C-Motion, Inc., Germantown, MD, USA). Marker positions and GRF were smoothed using a forward-reverse 4^{th} order low-pass Butterworth filter with a frequency cutoff of 10 Hz and 50 Hz, respectively, with seven frames reflected and a six-frame buffer. A six degrees of freedom link segment model was constructed for each subject from the static trial, and iterative Newton-Euler inverse dynamics was used to calculate forces and moments (Krupenevich et al., 2017). A 20 N threshold of the vertical ground reaction forces identified initial foot contact and toe off. Previous studies on running suggest 3-4 “trials” (strides) of data per subject per condition are minimally needed for stable and reliable results in running biomechanics (Bates, Dufek, & Davis, 1992; James, Herman, Dufek, & Bates, 2007). Data from at least three trials were processed for each speed of each subject, with an average of five trials per speed per subject. Velocity was determined using the stride length and the stride time between successive heel strikes.

Raw data from a representative subject that was used to calculate the VALR, peak free moment, and peak tibial load used to calculate the cumulative outcome variables are shown in Figure 2. VALR was calculated as the average slope of the vertical GRF vs. time between 20-80% of the time from initial contact to impact peak and scaled by body weight (BW) (Milner, Ferber, et al., 2006). When no impact peak was present, 13% of stance was used as a surrogate point to calculate loading rate (Blackmore, Willy, & Creaby, 2016). Free moment was scaled by bodyweight and height, and the peak absolute value during stance was determined (Milner, Davis, et al., 2006). Tibial load was calculated by first estimating Achilles tendon moment arm length as 20% of foot length, with foot length defined as the distance between the calcaneus and great toe markers along the long axis of the foot (Giddings, Beaupre, Whalen, & Carter, 2000), then dividing the plantarflexion ankle moment during stance by the moment arm estimate to calculate Achilles tendon force, and lastly by adding the Achilles tendon force to the axial component of the resultant inverse dynamics ankle force, with the tibial load also expressed on the long axis of the tibia. These calculations were performed for each measured stride, and the VALR, peak absolute free moment, and peak tibial load were averaged over strides to determine the ensemble averages used as outcome variables in all further calculations.

Cumulative load of the VALR, absolute free moment, and tibial load was calculated per-kilometer for two hypothetical conditions of running an arbitrary distance/mileage in training and expressed as the load accumulated per kilometer of running. Condition 1 was calculated assuming that all distance was performed at the normal speed v_{normal}. The number of steps required to cover 1 km was determined by dividing this distance by the step length of v_{normal}. For each outcome variable, the number of steps was multiplied by the variable's per-step magnitude to calculate the cumulative load. Condition 2 was calculated assuming that some distance was run at the slow speed v_{slow} and some at the fast speed v_{fast}, such that the average speed equaled v_{normal}. Specifically, the fraction of each kilometer run at the slow speed (d_{slow}) and the fast speed (d_{fast}) were:

$$T = \frac{d_{normal}}{v_{normal}} \quad [3.1]$$

$$d_{slow} = \frac{v_{fast} v_{slow} T - d_{normal} v_{slow}}{v_{fast} - v_{slow}} \quad [3.2]$$

$$d_{fast} = d_{normal} - d_{slow} \quad [3.3]$$

where $d_{normal} = d_{slow} + d_{fast} = 1$ km and T is the time spent running per km. Derivation of this equation is in Appendix 1. Cumulative load of the three outcome variables in the combined slow and fast running condition was then calculated by: i) dividing the distance proportion determined from equations 2a-c by the step length at the corresponding speed to obtain the number of steps at each speed, ii) multiplying the step number by the per-step magnitude of each variable, and iii) summing the slow and fast contributions of each load variable. Thus, both conditions had the same total distance, the same total time *T* spent running, and the same average speed, and differed only in the specific speed(s) used.

Statistical Analysis

Statistical analysis was done using a customized script in R (R Core Team, 2016). To check for differences in outcome variables between the subjects' self-selected speeds, within-subjects repeated measures ANOVAs compared speed, step length, VALR, free moment, and peak tibial load between self-selected slow, normal, and fast speeds. When the assumption of sphericity was violated, Greenhouse-Geisser corrections were reported for departures from sphericity (denoted by epsilon) of less than 0.75 (VALR, free moment) (Girden, 1992). For variables with a significant main effect of speed, post-hoc analysis was done using Tukey HSD with a Bonferroni correction for multiple comparisons, resulting in a critical α of 0.01 to achieve significant differences between speeds.

For each of the three outcome variables, the cumulative loads for both speed conditions were tested for assumptions of normality and homoscedasticity. When the assumptions were met a paired *t*-test was performed (VALR, tibial load), and for variables that violated these assumptions a Wilcoxon signed-rank test was used (free moment). Finally, a comparison of the contribution of slow and fast speeds to cumulative loads in Condition 2 was done using the appropriate *t*-test (VALR, tibial load) or Wilcoxon signed-rank test (free moment). Significance was determined by $\alpha=0.05$ for comparisons of cumulative load. Cohen's *d* effect sizes were calculated for all normal comparisons, where the numerator was the difference in means between the load-related variables for the two conditions, and the denominator was the pooled within sample standard deviation of the two conditions (Cohen, 1977). Wilcoxon signed-rank test correlation coefficient *r* was calculated by dividing the test statistic Z by the square root of the total number of observations.

Results

All subjects demonstrated a systematic increase in velocity as the self-selected speeds increased and were included in the analysis. The slow, normal, and fast self-selected running speeds averaged 2.70, 3.27, and 4.08 m/s, respectively. Speed, step length, VALR, peak absolute free moment, and peak tibial load were all greater at normal speed vs. slow speed and at fast speed vs. normal speed. Differences in magnitudes between speeds are shown in Figure 3, and the statistical significance and effect sizes are detailed in Table 3.1. There was a main effect of self-selected speed on running speed, step length, VALR, free moment, and tibial load (free moment: $p = 0.002$, all others: $p \leq 0.001$). Post-hoc Tukey HSD tests revealed that speed, step length, VALR, and tibial load values were significantly different between normal and fast speeds, slow and fast speeds, and slow and normal speeds (d = 0.40-3.18), with these variables increasing with increasing speed (Table 3.1). Per-step free moment values differed only in normal compared to fast speeds and slow compared to fast speeds, and did not differ significantly in slow compared to normal speeds (Table 3.1).

The proportions of slow and fast running required to equal normal speed over a hypothetical 1-km distance was 0.50±0.15 km of slow running and 0.50±0.15 km of fast running. Estimated cumulative VALR was significantly lower when running all distance at normal speed than at the combination of fast and slow running speeds (55,043±15,481 vs. 60,023±16,667 BW/s, $p < 0.001$, $d = 0.31$). Estimated cumulative free moment was not significantly different between the two running speed distributions (7,787±3,653 vs. 8,572±4,072 %BW•Ht, $p = 0.10$, $r = 0.18$), nor was estimated cumulative tibial load (5,792±854 vs. 5,772±827 BW, $p = 0.58$, $d = 0.02$) (Figure 3.4). For the combination of fast and slow speeds, the contribution of the slow speed to estimated cumulative tibial load was significantly greater than the contribution of the fast speed (Table 3.2, Figure 3.4). The contribution of slow and fast speeds to estimated cumulative load did not differ for VALR or free moment (Table 3.2, Figure 3.4).

Discussion

The purpose of this study was to compare estimated cumulative values of three running biomechanics variables related to tibial stress fracture (VALR, peak free moment, and peak axial tibial load) between two different proportions of running speed over an equal distance: (i) all distance run at a "normal" self-selected speed, and (ii) the same distance split between self-selected "slow" and "fast" speeds such that the average speed equaled the "normal" speed. As expected, running speeds were significantly different between runners' self-selected slow, normal, and fast speeds, and these differences were associated with concomitant increases in step length, peak VALR, peak free moment, and peak tibial load (Figure 3.3, Table 3.1). The effects of running speed on peak load magnitudes are similar to previous investigations, where faster running speed led to higher magnitude per-step loads (Hamill et al., 1983; Miller et al., 2014; Novacheck, 1998; Petersen et al., 2015).

Our first hypothesis was that the estimated cumulative loads of running all mileage at self-selected normal speed compared to a combination of self-selected slow and fast speeds would be similar over the same distance and at the same average pace. This hypothesis was partially supported: estimated cumulative free moment and tibial load were similar between the two speed distributions, however estimated cumulative VALR was significantly lower when all mileage was run at normal compared to the combination of slow and fast speed (Figure 3.4). In other words, a combination of slow and fast running speeds increased the estimated VALR accumulated per kilometer of distance compared to running at a single moderate speed, even when the average pace was equal. The present results have implications for how training load is quantified in running, and for the inclusion of fast running in training programs. Training errors, such as too much volume, too much intensity, or progressing volume or intensity too quickly, are often cited as the primary cause of injury in runners (Lysholm & Wiklander, 1987; Ramskov et al., 2018). Volume is typically quantified with weekly mileage. Intensity can be quantified in a variety of ways and is not necessarily synonymous with speed, but the average speed is a common metric (Hreljac et al., 2000). Reports on how volume, intensity, and progression affect injury risk do not show a clear association between these factors and injury (Hespanhol Junior et al., 2013; Hreljac et al., 2000; Nielsen et al., 2014; Ramskov et al., 2018). Hreljac et al. found no difference in mileage or average pace between injured and uninjured runners, i.e. there was no difference in volume or intensity between groups (Hreljac et al., 2000). In addition, equivalent increases in either volume or intensity caused no difference in running-related injury incidence after 24 weeks of training (Ramskov et al., 2018). Tibial stress fracture injury rate decreased with running distance progression up to 30% (Nielsen et al., 2014). Our results indicate that average running pace alone may not provide sufficient information on a runner's training to infer cumulative load since estimated cumulative VALR was different between conditions even though mileage and average running pace were the same. How or if cumulative load as we defined it here affects injury risk remains to be seen.

Our second hypothesis was that the slow and fast speeds would contribute similarly to the total cumulative load of the combined slow and fast condition. This hypothesis was also partially supported: slow and fast speeds contributed similarly to estimated cumulative

VALR and free moment, but slow running had a significantly greater contribution to estimated cumulative tibial load than fast running (Figure 3.4, Table 3.2). These results suggest that adding more fast running in a training program without also changing other aspects of training e.g. the amount of slow running will not necessarily increase cumulative load directly. Details of the entire training program including specific proportions of slow/easy and moderate pace runs need to also be considered. Future investigations into runners' training habits should include more detailed descriptions and histories of training programs beyond average running speed and total volume to avoid filtering out relevant program characteristics that may contribute to cumulative load.

There are currently no known relationships between high (or low) values of any particular cumulative biomechanical load and the risk for any particular running injuries. Studies on running biomechanics and retrospective or prospective injuries to date have focused on more tradition "peak" or "per-step" variables. However, cumulative load has a compelling theoretical basis for playing a causal role in tissue damage and failure (Baggaley & Edwards, 2017; Bertelsen et al., 2017; Edwards, 2018a; Edwards et al., 2009; Hreljac, 2004). If we assume high cumulative loads or an abrupt increase in cumulative loads are a risk factor for injury, the present results may partially explain why fast running in the form of interval training has not been associated with injury (Hespanhol Junior et al., 2013): it appears that the cumulative load from reasonable volumes of fast running is not particularly high. However, the present analyses are limited in that we did not model the relationship(s) between cumulative load, cumulative tissue damage, and positive or negative tissue adaptation. Such analyses could be informative of theoretical injury risk but would require much more sophisticated models.

Peak tibial load values were somewhat lower in the present than previous studies which reported ranges of 7.7 to 13 BW (Almonroeder et al., 2013; Burdett, 1982; Giddings et al., 2000; Sasimontonkul et al., 2007; Scott & Winter, 1990). It is likely that the differences in our estimates are due to differences in average speeds, ankle moment arm estimates, and calculation method. Our slow and normal average speeds were much lower (2.70 and 3.27 m/s, respectively) than those used in previous studies, where speeds ranged from 3.5 to 5.3 m/s. If we consider trials across all self-selected speeds where running velocity equals this range, per-step tibial load ranges from 5.1 to 12.2 BW (n = 58), which matches the velocity range and more closely matches previously reported peak tibial load values of 7.7-10.4 BW (n = 5) (Scott & Winter, 1990). We used a subject specific estimate based on percentage of foot length that averaged 0.053 m (Giddings et al., 2000), while others used a standard length of 0.05 m for all subjects (Almonroeder et al., 2013), or calculated a changing moment arm based on ankle range of motion throughout stance (Sasimontonkul et al., 2007). Post-hoc calculation of the tibial load using a standard 0.05 m ankle moment arm resulted in an average of 7.6 BW (range: 5.55-11.26 BW) for subjects running at 3.5 to 5.3 m/s, similar to the 7.7-10.8BW range reported by Scott & Winter (Scott & Winter, 1990). Additional analysis showed that the average ankle dorsiflexion angle at the point of peak tibial load was 24.7 degrees, 25.5 degrees, and 25.8 degrees at slow, normal, and fast speeds. The largest and smallest within subject between-speed differences were 8.5 and 2.8 degrees, respectively. Previous research shows the sagittal plane Achilles tendon moment arm may decrease up to 2 cm from 20-35 degrees of plantarflexion to 20-25 degrees of dorsiflexion (McCullough, Ringleb, Arai, Kitaoka, & Kaufman, 2011), so it is possible that a more detailed model of the Achilles tendon moment arm may affect the results. We also used a simplified method of estimating Achilles tendon force that assumed no contribution of any muscles other than the triceps surae to the ankle plantarflexion moment. The tibialis anterior has been shown to activate during the first 20% of ground contact (Sasimontonkul et al., 2007; Scott, Stephen, H., Winter, 1990), the peroneus longus activates in a similar pattern as the triceps surae muscles (Scott, Stephen, H., Winter, 1990), and the peroneals and other plantarflexor muscles contribute less than 1 BW to Achilles tendon force (Scott & Winter, 1990). Because the contribution of these and other muscles to the ankle moment is small, and because we were most concerned with how the peak loads changed with step length across speeds, we used a simpler Achilles tendon force estimate. The tibial loads here could be interpreted as the minimum theoretical loads, assuming factors like antagonistic co-contraction and agonistic force sharing are negligible at the range of speeds studies in these runners.

There are several other limitations to this study. First of these is the statistical strength of this study. Investigations into cumulative loads are relatively novel, therefore we do not have a large number of previous studies to guide the selection of statistical power and effect sizes for these specific variables. Per-step magnitudes of VALR, free moment, and tibial load have been studied in-depth on the basis of their association with tibial stress fracture injury history (Milner, Davis, et al., 2006; Milner, Ferber, et al., 2006). Because we are most interested in how the accumulation of these variables may also be associated with tibial stress fracture injury risk, we chose statistical power and effect sizes based on these stress fracture injury studies rather than investigations into the effect of running speed on cumulative load (Petersen et al., 2015).

Additionally, our results do not account for potential within- or between-run changes in running mechanics, muscle/tendon mechanics, structure-specific capacity, or metabolic factors that may cause changes in cumulative load experienced by runners within a run or as they perform runs over time. Most studies on cumulative load, including the present, have defined the "load per unit distance" using loads and stride lengths from fairly short distances of actual running in the lab (Edwards, 2018; Miller et al., 2014; Petersen et al., 2015) as opposed to measuring all steps within a distance that runners typically run (e.g. several miles), where factors such as fatigue and fluctuations in footstrike, speed, etc. may affect the actual load accumulated. Future investigations into how cumulative load is affected by related factors such as fatigue-related changes in running mechanics or changes in footstrike pattern with speed may further our understanding of how modifiable gait mechanics affect cumulative load in running.

A final limitation to both the present work and recent cumulative load research in general is that the causal relationship between injury and cumulative loading from any particular mechanical variable is unknown and is largely theoretical to date (Edwards, 2018; Edwards et al., 2009; Hreljac, 2004; Miller et al., 2014). Our results show that while faster running speed does not necessarily increase the cumulative loading of tibial stress fracture-related variables, it does increase the peak values of these variables and it is these peak values that have been more closely associated with actual injuries (Davis et al., 2016; Hreljac et al., 2000; Milner, Davis, et al., 2006; Milner, Ferber, et al., 2006; Pohl et al., 2008). Which "form" of these variables (e.g. peak, cumulative) is the best predictor of injury and has the most direct causal role in injury mechanisms is in need of further investigation. Prospective studies from different labs have shown inconsistent results between studies concerning which peak loads per step are associated with injury (Davis et al., 2016; Messier et al., 2018; Napier et al., 2018). Assessments of cumulative loads would not necessarily show more consistent results, but this possibility seems worthwhile of investigation.

In conclusion, when average running pace and distance are equal, a combination of slow and fast speeds leads to greater estimated cumulative VALR and similar magnitudes of estimated cumulative free moment and tibial load when compared to running at all normal speed. However, the greater cumulative VALR resulted from greater loading during slow running compared to fast running. These results suggest volume and average pace are not sufficient metrics for tracking cumulative load when speed fluctuated substantially over the course of a training volume or even within a single run.

Table 3.1

Comparisons of Running Kinematics and Kinetics Between Speeds

	normal vs. fast	slow vs. fast	slow vs. normal
Speed (m/s)			
Difference	-0.81	-1.37	-0.56
p-value, ES	<0.001, 1.75	<0.001, 3.18	<0.001, 1.51
Step Length (m)			
Difference	-0.21	-0.39	-0.18
p-value, ES	<0.001, 1.36	<0.001, 2.83	<0.001, 1.38
VALR (BW/s)			
Difference	-24.3	-33.3	-9.0
p-value, ES	<0.001, 1.04	<0.001, 1.43	0.004, 0.52
Tibial Load (BW)			
Difference	-0.45	-0.96	-0.51
p-value, ES	<0.001, 0.40	<0.001, 0.85	<0.001, 0.46
Free Moment (%BW*Ht)			
Difference	-3.46	-4.16	-0.70
p-value, ES	0.001, 0.43	<0.001, 0.53	1, 0.09

Note. The numeric between-speed differences are the average of the slower speed minus the faster speed, and ES is Cohen's *d* effect size.

Table 3.2

Combined Cumulative Loads and Contributions of Slow and Fast Running to the Combined Condition

	Combined	Slow	Fast	*p*-value	ES
VALR (BW/s)	60024 ± 1667	28085 ± 12829	31939 ± 12574	0.163	0.43
Free Moment (%BW*Ht)	8572 ± 4072	4167 ± 1919	4405 ± 3050	0.810	0.01
Tibial Load (BW)	5772 ± 827	3171 ± 1031*	2602 ± 737	0.004	1.10

Note. Combined Mean ± SD, Mean ± SD by speed, significance and effect sizes (ES) between speeds. Cohen's *d* was used for effect sizes for VALR and Free Moment, and *r* was used for Tibial Load.
* Indicates significant difference from fast speed determined by a Wilcoxon signed rank test.

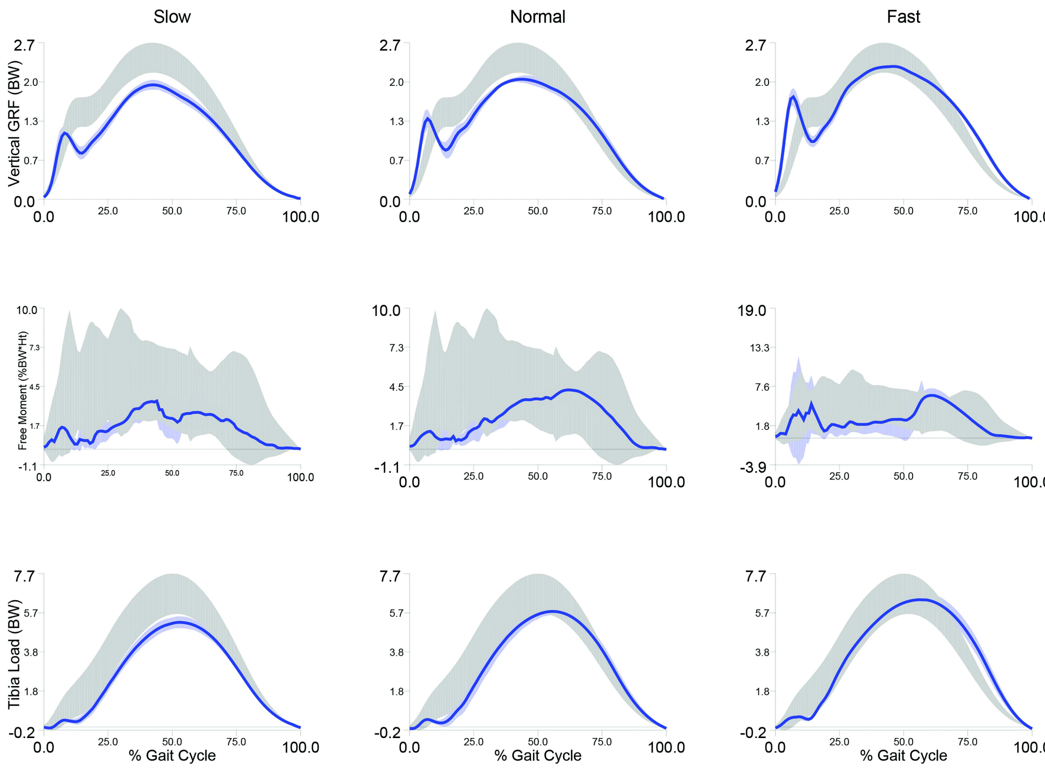

Figure 3.1. Time series data for a representative subject for vertical GRF (top row), absolute free moment (middle row), and axial tibial load (bottom row). Each plot shows the mean and standard deviation of the representative subject (blue) and the global standard deviation (all subjects and all speeds, gray).

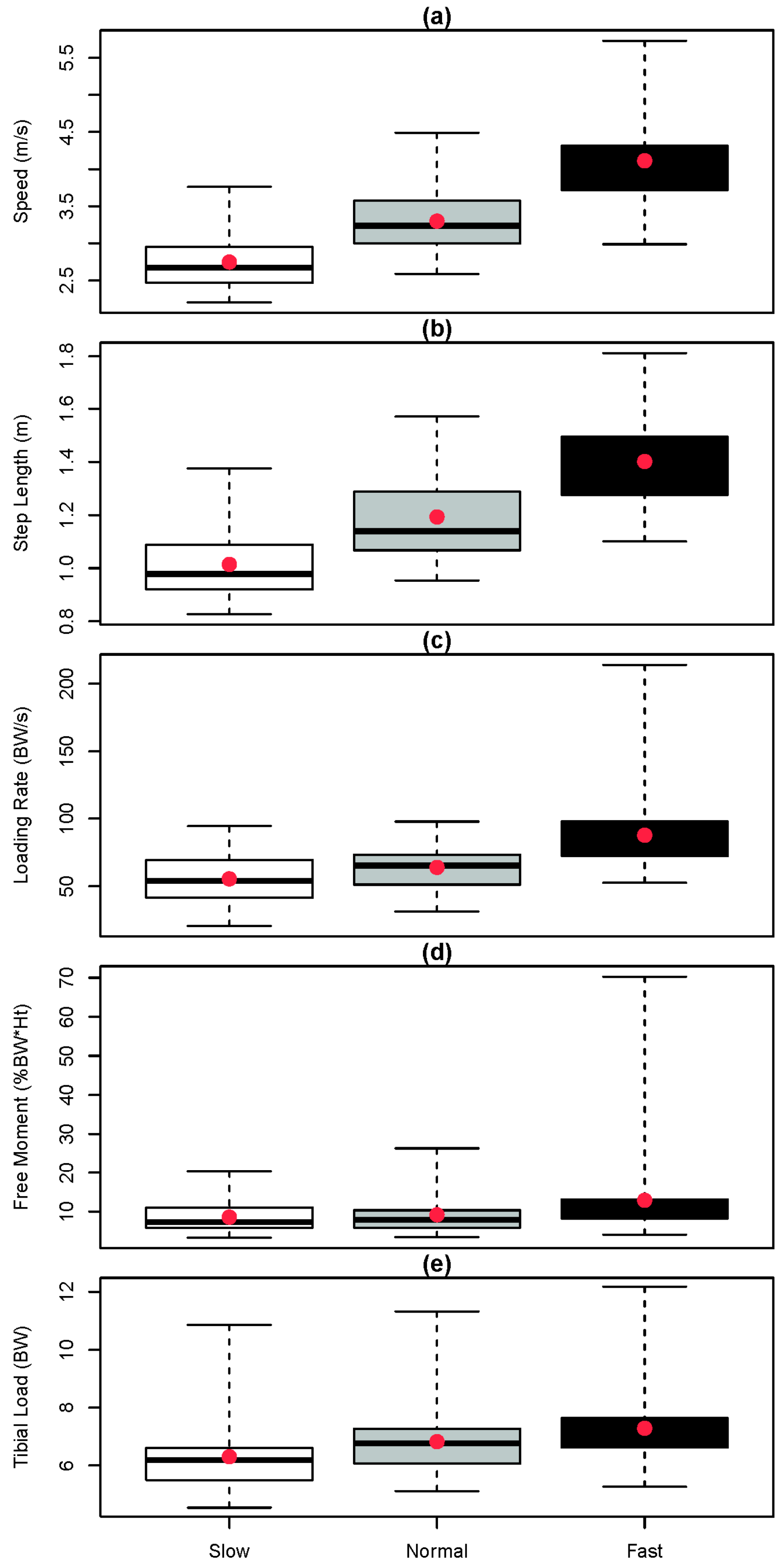

Figure 3.2. A boxplot of the kinematics and per-step kinetics at slow, normal, and fast speeds. The mean and median are represented by the red circle and horizontal line within each box, respectively. The whiskers extend to the range of each variable.

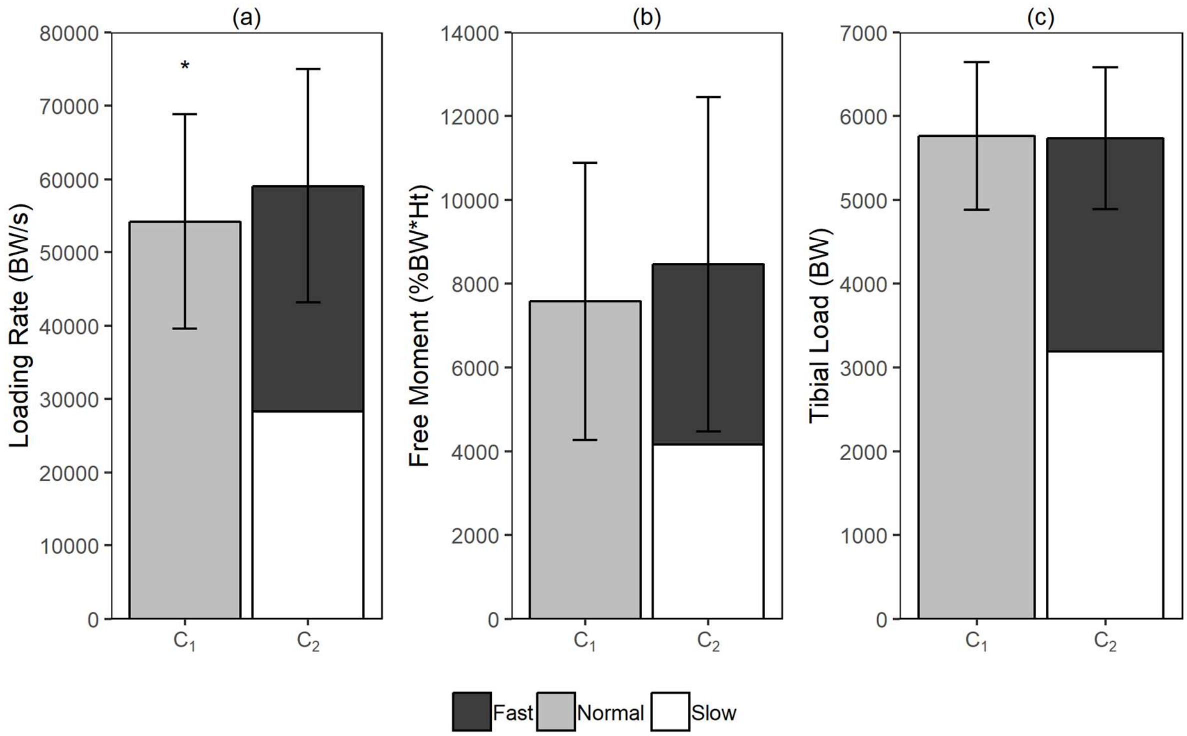

Figure 3.3. A boxplot of the contribution of fast and slow speeds to VALR, peak absolute free moment, and peak tibial load. The mean and median are represented by the red circle and horizontal line within each box, respectively. The whiskers extend to the range of each variable.

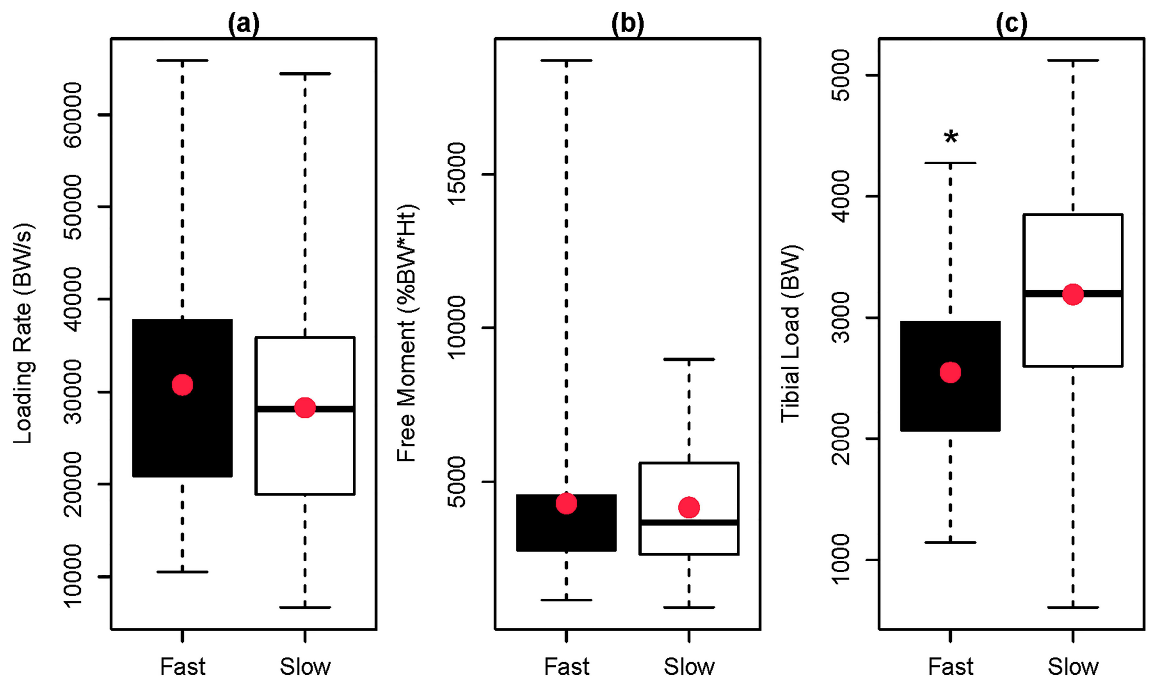

Figure 3.4. A boxplot of the contribution of fast and slow speeds to VALR, peak absolute free moment, and peak tibial load. The mean and median are represented by the red circle and horizontal line within each box, respectively. The whiskers extend to the range of each variable.

Chapter 4: Novice runners maintain cumulative loads during steady-state running

Introduction

Running for exercise, recreation, and health benefits has a low barrier to participation, and has increased in popularity in recent decades, especially for women (Running USA, 2019; Scheerder & Vos, 2011). The increase in female runners likely has public health benefits, as running is effective in improving chronic disease outcomes (Williams, 2008). However, running-related pain and injury rates are as high as 64.6% (Reinking et al., 2013), and novice runners have higher injury incidence compared to more experienced runners (Taunton et al., 2003; Videbæk et al., 2015). Prospective injury incidence is also higher in women than men (Taunton et al., 2002), and female athletes have 10 times the relative risk of developing a stress fracture compared to the general population (Battaloglu, 2011). Stress fracture injury risk is predicted to be highest between 1 to 2 months of beginning a new sport activity (Taylor & Kuiper, 2001), making novice female runners a particularly high risk group. Many studies have attempted to describe factors that may explain the higher risk of injury in novice runners and females, such as training habits, running experience (Reinking et al., 2013), and biomechanical factors (Chan et al., 2018; Maas et al., 2018) with inconsistent results. The increased participation of female runners (Scheerder & Vos, 2011) and higher incidence of running-related injuries in female versus male runners (Taunton et al., 2002) suggests a need to better understand how training habits, experience, and biomechanics interact in female runners, especially those relatively new to running.

Biomechanical studies of running injuries often focus on peak loads during running to explain injury risk or injury development (Chan et al., 2018; Adam C. Clansey et al., 2012; Gerlach et al., 2005; Milner, Ferber, et al., 2006; M. R. Paquette & Melcher, 2017). More recently, studies have applied fatigue-failure concepts from materials science by estimating the cumulative loads the body experiences during running (Hunter, Garcia, Shim, & Miller, 2019; Petersen et al., 2015). A number of recent studies have also modeled how the relationship between running habits and mechanical fatigue may affect injury risk, suggesting there is a connection between running speed, running volume, and running mechanics (Chen et al., 2016; Edwards et al., 2009, 2010). Cumulative load estimates and mechanical fatigue models both consider the number of loading cycles, or steps, and the peak loads experienced during running. However, there is currently no established association between higher or lower cumulative loads with injury development or prevention. “Fatigue” in the previously mentioned studies refers to the materials science definition of mechanical fatigue (degradation of material properties with cyclical loading) rather than the medical definition more common in exercise science that describes a decline in performance or change in biomechanics to maintain performance. This decline in performance due to prolonged duration activity has been described as performance fatigability (Enoka & Duchateau, 2016). Previous studies that have found decreases in step length due to prolonged running (Gerlach et al., 2005; Maas et al., 2018; Willson & Kernozek, 1999) suggest that a running bout of sufficient duration may also affect the likelihood of developing an injury since, according to fatigue-failure mechanics, the interaction of the number of loading cycles and the load magnitude may lead to degradation of body structures and subsequent injury.

Performance fatigability contributes to fatigue in running with associated changes in perceived fatigability, the physiological and psychological factors that affect the sensations a runner experiences (Enoka & Duchateau, 2016). Perceived fatigability can be quantified by perceived exertion or physiological metrics such as heart rate response or blood lactate accumulation (Enoka & Duchateau, 2016). Regardless of experience or fitness, heart rate (HR) increased gradually during steady-state exercise (Foster et al., 2001b; Oyono-Enguelle et al., 1990) and blood lactate accumulation initially spiked after the exercise onset, but gradually decreased towards the end of exercise at lower intensities (Oyono-Enguelle et al., 1990). Both HR and blood lactate accumulation may be important factors in performance fatigability since they provide feedback to an individual on exercise intensity and affect rating of perceived exertion (RPE) (Foster et al., 2001b). The relationship between various metrics used to quantify fatigability, i.e. RPE, HR, blood lactate accumulation, and modifications of gait mechanics variables associated with tibial stress fracture injury in novice female runners throughout a run is unknown. Limited research on female runners specifically indicates that women may respond to prolonged running differently from men (Gerlach et al., 2005), but most performance fatigability studies investigating stress fracture risk variables use well-trained or active males (Derrick et al., 2002; Mizrahi, Verbitsky, & Isakov, 2000b; Paquette & Melcher, 2017), or a mix of males and females (Maas et al., 2018). This gap in knowledge is important because identifying a relationship between easy to measure metrics such as RPE, HR, and blood lactate accumulation, and difficult to measure metrics such as the vertical instantaneous loading rate (VILR), free moment, and axial tibial load, may improve the ability of commercially available wearable devices such as accelerometers used to measure tibial shock to extrapolate load-related information that contributes to injury risk (Willy, 2018).

Therefore, the purpose of this study was to compare the cumulative load per kilometer of the VILR, peak free moment, peak axial tibial load, and peak tibial shock for each kilometer of a prolonged, sub-threshold run to volitional fatigue. Untrained runners show an increase in cadence and decrease in step length when fatigued (Willson & Kernozek, 1999) but if or how loading variables will change with fatigue is unclear. Therefore, we expected runners to maintain step frequency and peak loads for a portion of the run, after which step frequency would gradually increase and peak loads would remain constant. We hypothesized that cumulative loads per kilometer would increase during the run due to a fatigue-related increase in step frequency. A secondary purpose was to determine if there is relationship between perceived fatigability metrics and cumulative loads per kilometer. HR and RPE continuously increase during steady-state exercise, while blood lactate accumulation response varies based on exercise intensity (Oyono-Enguelle et al., 1990). Therefore, we expected that HR and RPE would positively correlate with cumulative loads per kilometer but not peak loads, and there would be no relationship between blood lactate accumulation and peak loads or cumulative loads per kilometer.

Methods

Participants

Power analysis indicated that 20 subjects are needed to detect correlations of $r = 0.55$ or greater, therefore 20 healthy novice female runners were recruited to participate (Table 4.1). This number of subjects is consistent with previous investigations on the effects of fatigue on tibial acceleration, loading rates, and free moment that have used sample sizes of

13 to 22 and achieved effect sizes ranging from 0.2 -1.49 (Clansey et al., 2012; Davis et al., 2016; Pohl et al., 2008). Concerning the definition of “healthy novice”, inclusion criteria were (1) females 18-40 years of age, (2) less than 2 years lifetime running experience and have run at least 8 km per week for the past 3 months (Chan et al., 2018), (3) have no competitive running experience e.g. training for a race with a minimum-time goal, (4) run with a rearfoot strike pattern, (5) have had no major surgery or condition that would affect gait patterns within the past 6 months, (6) are considered at low risk for coronary artery disease according to American College of Sports Medicine risk stratification, (7) have experience running on a treadmill. Approval was obtained from the local Institutional Review Board, and data collection took place at the Spaulding National Running Center in Cambridge, MA. Participants refrained from intense exercise for 48 hours prior to participation, and any planned exercise for 24 hours prior to their visit to minimize effects of fatigue from recent physical activity. Each participant gave written informed consent and underwent a brief treadmill run to determine footstrike pattern and running speed for the prolonged run. Footstrike pattern was assessed visually using high-speed 2-dimensional video, and only runners with a rearfoot strike pattern were included in the study. Participants completed a demographic questionnaire about exercise habits and injury history, running shoes, coronary artery disease risk stratification (Appendix 1), and female athlete triad risk (De Souza et al., 2014).

Experimental Setup

Data was collected in a single visit that lasted approximately 2 hours. Participants wore their own shoes, shorts, and sports bra/tank top. Height and foot length was recorded. Participants wore 70 reflective markers on their feet/ankle (distal, proximal and lateral heel, hallux, first and fifth metatarsals, lateral and medial malleoli), knees (medial and lateral tibial plateaus and femoral epicondyles), 4-cluster markers on shanks and thighs, greater trochanters, pelvis (anterior and posterior superior iliac spines, iliac crests, sacrum), trunk (sternal notch, sternoclavicular joints, 7^{th} cervical vertebra), arms (acromioclavicular joints, posterior upper arm, medial and lateral humeral condyles, wrist), and head (2 anterior, 2 posterior, temples) to identify joint locations and movement. An accelerometer (IMeasureU, Vicon, Denver, CO, USA) was placed on the anteromedial surface of the right and left tibia using an elastic strap. Participants wore a heart rate monitor strap around the torso paired with a smartphone app to record heart rate every second throughout the run (Polar H10 Heart Rate Sensor, Polar Electro Inc., Bethpage, NY, USA).

Participants walked and ran on an instrumented treadmill (AMTI, Watertown, MA, USA) which measured three-dimensional ground reaction forces (GRF) sampling at 1000 Hz. Marker positions were captured using an 8-camera motion capture system (VICON, Centennial, CO, USA) sampling at 200 Hz. Participants first performed a static calibration trial by standing still on the rear section of the treadmill belt with feet shoulder width apart and arms abducted to 90° for 1 second, after which calibration markers (first metatarsal, all knee markers, greater trochanters, iliac crests, acromioclavicular joints, medial humeral condyle, temples) were removed.

Testing began with a 3-minute walking warm-up. Treadmill speed was set to 3.0 miles per hour and increased quickly until subjects reported a brisk pace sufficient to warm-up. At the end of the 3-minute warm-up, treadmill speed was immediately increased to the speed participants described as the running speed they would choose for their longest weekly run. The run terminated when participants reached fatigue, defined as the point when they subjectively report that they are unable or unwilling to complete another kilometer. Borg scale RPE, blood lactate measurements, and 16 seconds of motion capture data were collected in the last 90 seconds of the walking warm-up, between the initial 1:30-3 minutes of the run, and during the last 90 seconds of each kilometer during the run. Blood lactate levels were measured using a portable blood lactate analyzer (Lactate Plus Meter, Nova Biomedical, Waltham, MA, USA) on a small amount of blood obtained by a finger prick. Upon run termination participants were encouraged to walk until heart rate and breathing returned to comfortable levels.

Data Reduction

Motion capture data was processed using Visual3D software (C-Motion, Inc., Germantown, MD, USA). Marker positions, GRF, and accelerometer data were smoothed using a forward-reverse 4th order low-pass Butterworth filter with cutoff frequencies of 10 Hz, 50 Hz, and 50 Hz respectively. A six degrees of freedom linked segment model was constructed for each subject from the static trial, and iterative Newton-Euler inverse dynamics was used to calculate forces and moments (Krupenevich et al., 2017). A 20 N threshold of the vertical ground reaction forces identified initial foot contact and toe off. An average of 22 steps per kilometer were used to estimate outcomes at each kilometer for each subject.

Figure 4.1 shows time series data from a representative subject that was used to calculate the VILR, free moment, axial tibial load, and tibial shock. VILR was calculated as the greatest slope of the vertical GRF between successive points from 20-80% of the time from initial contact to impact peak and scaled by body weight (BW) (Davis et al., 2016). When no obvious impact peak was present, 13% of stance was used as a surrogate point to calculate loading rate (Blackmore et al., 2016). Free moment was scaled by bodyweight and height, and the peak absolute value during stance was determined (Milner, Davis, et al., 2006). Axial tibial load was calculated by first estimating Achilles tendon moment arm length as 20% of measured foot length. Then the plantarflexion ankle moment during stance was divided by the moment arm estimate to calculate Achilles tendon force. Lastly, the Achilles tendon force was added to the axial component of the resultant ankle force, with the tibial load also expressed on the long axis of the tibia. Tibial shock was identified as the peak magnitude during stance. These calculations were done for each step, and the average VILR, peak absolute free moment, peak axial tibial load, and peak tibial shock were determined for the beginning of the run and each kilometer completed, and subsequently used to estimate cumulative load per kilometer.

Data Analysis

Cumulative Load

Cumulative load of the VILR, absolute free moment, axial tibial load, and tibial shock at the beginning of the run and for each kilometer completed were calculated as (Hunter et al., 2019):

$$C_i = \frac{d}{L_i} M_i \qquad [4.1]$$

where d is 1000 meters, i is the kilometer number, L is step length in meters, and M is the magnitude of the outcome variable (VILR, peak absolute free moment, peak axial tibial load, or tibial shock) at kilometer i.

Estimated Maximal Oxygen Consumption

Continuous heart rate data from the prolonged run was downloaded from a generic Polar Flow account created for this study. Maximal oxygen consumption (VO_2 max) was estimated for each subject according to a predictive equation (Vehrs, George, Fellingham, Plowman, & Dustman-Allen, 2007), and cardiorespiratory fitness was classified based on ACSM guidelines (Riebe, Ehrman, Liguori, & Meir, 2018). Average heart rate per-kilometer at self-selected running pace was also calculated.

Statistical Analysis

Statistical analysis was done using a customized script in R (Team, 2020). No variables met assumptions of normality; therefore nonparametric tests were performed. High tibial loads are assumed to be associated with greater tibial stress fracture injury risk (Edwards et al., 2009, 2010). Therefore right and left side axial tibial loads were compared using a Wilcoxon Test to identify differences between sides. Axial tibial loads were similar on both sides ($p = 0.82$), so only the dominant leg was analyzed further. Spearman's rho (r_s) was calculated to determine the relationship between run distance and step frequency, run distance and peak loads, and run distance and cumulative loads per kilometer. Spearman's rho was also calculated to determine the relationship between load outcomes and perceived fatigability outcomes. Specifically we tested the correlation between peak loads and HR, cumulative loads per kilometer and HR, peak loads and blood lactate concentration, cumulative loads per kilometer and blood lactate concentration, peak loads and RPE, and cumulative loads per kilometer and RPE.

Results

Participants ran at an average treadmill speed of 6.1 mph (2.7 m/s) and completed an average of 5 kilometers of running. Additional details of participant demographics and running speeds can be found in Table 4.1. Descriptive information of each outcome is detailed in Table 4.2. Figure 4.2 and Figure 4.3 show step frequency and peak loads at each kilometer for each subject, and cumulative loads at each kilometer for each subject, respectively. Correlation and significance values for all tests performed are in Table 4.3, and a summary of significant correlations is in Figure 4.4. There was no relationship between run distance and step frequency, run distance and any peak loads, or run distance and any cumulative loads per kilometer (Figure 4.3, Table 4.4).

RPE increased from the beginning to the end of the run ($r_s = 0.68$, $p < 0.001$) (Figure 4.5-A). Peak free moment was positively correlated to RPE ($r_s = 0.18$, $p = 0.04$), but there was no relationship between VILR, peak tibial load, or peak tibial shock and RPE. There was also no relationship between any cumulative loads per kilometer and RPE.

HR also increased from the beginning to the end of the run ($r_s = 0.42$, $p < 0.001$) (Figure 4.5-B). Peak free moment was positively correlated to HR ($r_s = 0.21$, $p = 0.05$) and peak tibial shock was negatively correlated to HR ($r_s = -0.26$, $p = 0.01$). There was no relationship between VILR or peak tibial load and HR. Cumulative VILR ($r_s = -0.24$, $p = 0.02$), cumulative tibial load ($r_s = -0.45$, $p < 0.001$), and cumulative tibial shock ($r_s = -0.25$, $p = 0.02$) were negatively correlated to HR, but there was no relationship between HR and cumulative free moment (Figure 4.3).

There was no relationship between blood lactate accumulation and run distance (Figure 4.5-C). Peak free moment was positively correlated to blood lactate accumulation ($r_s = 0.20$, $p = 0.03$), but there was no relationship between VILR, peak tibial load, or peak tibial shock and blood lactate accumulation. Cumulative free moment was positively correlated to blood lactate accumulation ($r_s = 0.20$, $p = 0.03$) and cumulative tibial load was negatively correlated to blood lactate accumulation ($r_s = -0.21$, $p = 0.02$). There was no relationship between cumulative VILR or cumulative tibial shock and blood lactate accumulation (Figure 4.3-C).

Discussion

The purpose of this study was to compare cumulative load of the VALR, peak free moment, peak axial tibial load, and peak tibial shock for each kilometer of a run to volitional fatigue in novice female runners. We expected that step frequency would increase and peak loads would be maintained throughout the run. Peak loads were maintained throughout the run as we expected, however step frequency also did not change significantly. Our first hypothesis was that the expected increase in step frequency and maintenance of peak loads would lead to an increase in cumulative loads per kilometer. This hypothesis was not supported. Since step frequency and peak loads were both maintained throughout the run there was no effect of run distance on cumulative loads per kilometer.

The secondary purpose of this study was to determine if there was a relationship between the perceived fatigability metrics RPE, HR, and blood lactate accumulation and cumulative loads per kilometer. As we expected, RPE and HR increased continuously throughout the run, and blood lactate accumulation did not show a linear increase with run distance (Foster et al., 2001b). No per-kilometer cumulative load variables were positively correlated to RPE or HR. Rather, cumulative VILR, cumulative tibial load, and cumulative shock were negatively correlated to HR and there was no relationship between any cumulative loads per kilometer and RPE. In addition, we found that peak free moment was positively correlated to RPE and HR, and peak tibial shock was negatively correlated to HR. We also found that peak free moment and cumulative free moment were positively correlated to blood lactate accumulation, and cumulative tibial load was negatively correlated to blood lactate accumulation.

The magnitudes of VILR, peak tibial load, peak free moment, and tibial shock are similar to previous investigations where running speeds were similar to the speeds runners selected in the current study (2.2-3.6 m/s) (Gerlach et al., 2005; Hunter et al., 2019; Milner, Davis, et al., 2006). The consistent increase in HR and RPE that our participants experienced is also consistent with previous investigations (Foster et al., 2001b; Oyono-Enguelle et al., 1990), however blood lactate accumulation response differed in our participants compared to well-trained participants exercising at moderate relative intensity (Oyono-Enguelle et al., 1990). We did not see an initial spike in blood lactate accumulation, which usually occurs within the first 10 minutes of steady state exercise and would have occurred between kilometer 0 and 2 in our participants. It is possible that the spike occurred but was not detected since blood lactate measurements were collected several minutes apart. We also did not see a gradual decline in blood lactate accumulation throughout the run. The lack of decline in blood lactate accumulation could be a result of the participants' fitness status, since training improves the clearance of blood lactate during exercise, or because exercise duration was not sufficient for the decline to occur (Oyono-Enguelle et al., 1990). In addition, some data points may be erroneous due to sensitivity of the lactate sensor to the volume of blood in a sample and difficulties of collecting finger stick samples during running.

There are several potential explanations for the runners' ability to maintain step frequency throughout the run although we expected an increase similar to previous studies (Girard, Millet, Slawinski, Racinais, & Micallef, 2013; Willson & Kernozek, 1999).

Previous studies of fatigue typically use high relative exercise intensity, such as ventilatory, anaerobic, or lactate threshold (Clansey et al., 2012, 2016; Mizrahi, Verbitsky, Isakov, et al., 2000), or 5k race pace (Derrick et al., 2002; Maas et al., 2018), and asked runners to run to exhaustion often defined as an RPE of at least 17 (Dierks et al., 2010; Maas et al., 2018). We asked runners to select their long run pace and run until they felt like they would normally stop at that pace in order to reflect the pace and intensity most similar to a large proportion of their total training mileage. It is possible that runners did not reach sufficient fatigue to elicit changes in gait mechanics. However, novice runners running to fatigue at their 5k pace ran 28 minutes (Maas et al., 2018) compared to an average of 32 minutes in this study. Our participants reached a maximum RPE rating of 16 (range: 14-19), suggesting that our participants reached similar levels of perceived intensity to participants in other fatigue studies that used more experienced runners and/or faster running speeds (Dierks et al., 2010; Maas et al., 2018). Considering the previously mentioned studies where runners ran to exhaustion but did not consistently alter temporospatial or mechanical gait variables, it is difficult to conclusively state the lack of significant gait adjustments in the current study's variables is directly due to the absence of fatigue.

Relatedly, while the condition measured here was intended to represent the majority of participant's typical running and presumably the majority of their typical cumulative load from running, there is no certainty that this purpose was necessarily achieved (e.g. subjects may have run faster or longer than they typically do), and it does not account for loads accumulated from other types of running, e.g. intense workouts, or from other modes of physical activity. Confidently assessing these issues would likely require "real-world" monitoring of running and general movement of the participants.

Determining the relationship between peak and cumulative loads and HR, RPE, and blood lactate accumulation was a novel attempt to determine if runners and coaches could infer potential injury related gait metrics from other metrics that are easily measured during a training run. However, the utility and applicability of these relationships is contingent upon a relationship between cumulative loads per kilometer and both run distance and injury risk. Regarding the relationship between cumulative loads per kilometer and run distance, we did not find any relationship between cumulative load variables and run distance. Although HR was correlated with cumulative tibial load per kilometer and cumulative VILR per kilometer, these variables themselves did not have a relationship with run distance. In addition, had cumulative loads per kilometer increased as we expected it is possible that the correlations between HR and cumulative loads would not be present. Tibial shock is relatively easy to measure in the field with affordable and simple commercial technology (Willy, 2018). Therefore, based on the current results, the negative correlation we found between HR and tibial shock may be useful to indicate that runners are maintaining gait mechanics. Future studies are warranted to determine if a fatigue breaking point could be identified when the relationship between HR and tibial shock changes to define either training intensity or duration thresholds.

Regarding cumulative loads per kilometer and injury risk, there is a nonlinear relationship between cumulative loads and cumulative damage (Edwards, 2018), and whether the lack of increase in cumulative loads per kilometer with fatigue translates to an absence of elevated injury risk is unknown. This lack of a relationship between cumulative load and injury risk is a main limitation of this and all running related research studies on cumulative loads (Edwards, 2018; Hunter et al., 2019; Petersen et al., 2015). Cumulative damage increases over time with higher running volume but shorter step length can mitigate this increase (Edwards et al., 2009) suggesting that increasing the number of steps but decreasing peak loads, which occurs when running speed decreases (Hunter et al., 2019) may decrease injury risk. The relationship between peak loads and number of loading cycles could also result in a change in injury risk with non-significant changes in gait mechanics throughout a run or over a period of training. We found a negative relationship between tibial load and run distance (r_s = -0.14, p = 0.12). Although this relationship was not significant, damage is sensitive to small changes in peak loads so it is possible that even these small changes could affect the amount of damage over the course of a run. When cumulative load estimates are weighted to account for the nonlinear relationship between cumulative loads and cumulative damage, estimates of injury risk from cumulative loading outcomes alone are promising (Kiernan et al., 2018). However, more research on how these estimates apply to different populations of athletes under different training conditions are warranted.

A final limitation to this study is that differences between the lab environment and runners' true running environment may have influenced the loads runners accumulated. Running outside often requires running up or down various grades which will also affect speed, kinematics, peak loads and subsequent cumulative loads that steady-state, zero grade treadmill running does not account for (Matijevich et al., 2019). In addition, as runners become fatigued it is common for running speed to decrease when they run autonomously (Girard et al., 2013). Participants ran on an instrumented treadmill at a self-selected constant pace, though it is possible that they would have chosen to continue if given the option to decrease running speed. Running at a slower speed causes peak loads and step length to decrease, however these decreases are associated with an increase in cumulative loads

(Hunter et al., 2019; Petersen et al., 2015). It is likely then that runners who decrease running speed over the course of a run would experience an increase in cumulative load. In order to reproduce the intensity and duration of each runner's most typical long run, we also allowed runners to determine when to stop rather than provide them with an external goal of a specific time, distance, or RPE, (Clansey et al., 2012, 2016; Maas et al., 2018; Paquette & Melcher, 2017). The level of performance fatigability our participants experienced may apply to the majority of a runner's total volume of running, since most training programs recommend large proportions of slow running (Stöggl & Sperlich, 2014). However, the effect of consecutive days of running, whether at relatively slow or fast speeds, may affect performance fatigability during a single run or over the course of a training program. Allowing the runners to stop volitionally also limits the applicability of our results when runners are completing unusual distances, such as when first undertaking a half-marathon or marathon training program, or completing a new race distance for the first time. Providing an external goal may have motivated runners to run further and may have led to larger magnitude changes in either step frequency or peak loads at their chosen speed. Our results suggest that runners may decrease running speed as a mechanism to moderate peak loads as a response to fatigue, and stop running when decreasing speed is not possible.

In conclusion, when novice female runners ran at a steady self-selected pace to fatigue, step frequency, cumulative VILR, cumulative free moment, cumulative tibial load, and tibial shock remained similar throughout the run. These results suggest that runners choose to stop running prior to experiencing altered gait mechanics. The present results also suggest that fatigue-related changes in gait resulting in increased peak or cumulative loads in the latter kilometers of 'easy' runs are not likely a major injury risk factor. However, because cumulative damage is sensitive to both peak loads and loading cycles, examining how cumulative load per kilometer affects injury risk is worthwhile. In addition, tracking HR and tibial shock may be an effective way to determine the onset of fatigue during outdoor training runs.

Table 4.1

Participant Characteristics

	Mean (SD)	Range
Age (years)	25 (6)	18-38
Height (cm)	165.2 (6.9)	150.9-176.4
Mass (kg)	64.0 (10.3)	43.3-84.9
Running Experience (months)	16 (9)	3-36
Running Exposure (miles/wk)	12.7 (6.1)	4.5-25.5
Walk Speed (mph)	3.5 (0.4)	3.0-4.0
Run Speed (mph)	6.1 (0.7)	5.0-8.0
Run Distance (km)	5.0 (1.6)	3.0-8.0
Estimated VO_2 max (ml/kg/min)	45.8 (4.1)	37.5-53.5
Fitness Ranking (percentile)	79 (13)	45-95

Table 4.2

Gait Mechanics Outcomes

	Right	Left
	Mean (SD)	
Step Frequency (steps/min)	174 (9)	174 (9)
VILR (BW/s)	57.4 (17.0)	57.9 (16.0)
Free Moment (%BW*Ht)	8.3 (2.6)	8.6 (2.4)
Tibial Load (BW)	7.4 (0.8)	7.4 (0.8)
Tibial Shock (g)	4.1 (1.5)	4.1 (1.4)

Table 4.3

Correlation Results: Gait Mechanics vs. Distance and Gait Mechanics vs. Performance and Perceived Fatigability

		Distance		Rating of Perceived Exertion		Heart Rate		Blood Lactate Accumulation	
		r_s	p	r_s	p	r_s	p	r_s	p
Peak	Step Frequency (steps/min)	0.04	0.69	--	--	--	--	--	--
	VILR (BW/s)	**-0.15**	**0.1**	0.07	0.44	-0.06	0.6	0.09	0.32
	Free Moment (%BW*Ht)	-0.01	0.91	**0.18**	**0.04**	**0.21**	**0.05**	**0.2**	**0.03**
	Tibial Load (BW)	-0.14	0.12	0.1	0.25	0.02	0.84	-0.14	0.14
	Tibial Shock (g)	-0.14	0.11	0.02	0.86	**-0.26**	**0.01**	0.02	0.85
Cumulative	VILR (BW/s)	-0.1	0.27	-0.06	0.5	**-0.24**	**0.02**	0.07	0.47
	Free Moment (%BW*Ht)	0.03	0.75	0.13	0.16	0.13	0.22	**0.2**	**0.03**
	Tibial Load (BW)	-0.03	0.77	0.02	0.85	**-0.45**	**<0.001**	**-0.21**	**0.02**
	Tibial Shock (g)	-0.11	0.24	-0.02	0.79	**-0.25**	**0.02**	0.02	0.84

Note: Significant correlations are in bold text.

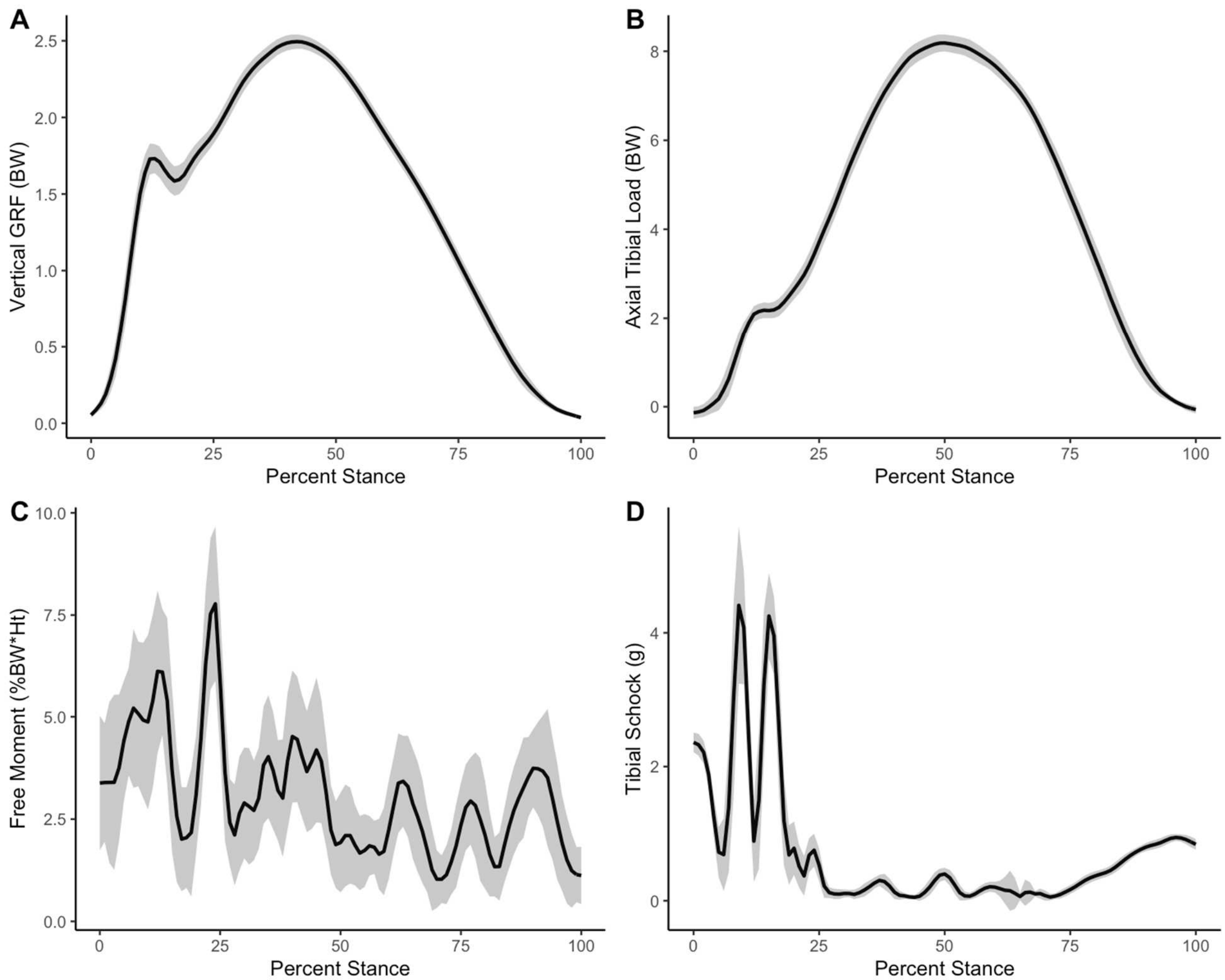

Figure 4.1. Data from a representative participant showing the time series data used to calculate VILR (A), and identify peak tibial load (B), peak free moment (C), and peak tibial shock (D).

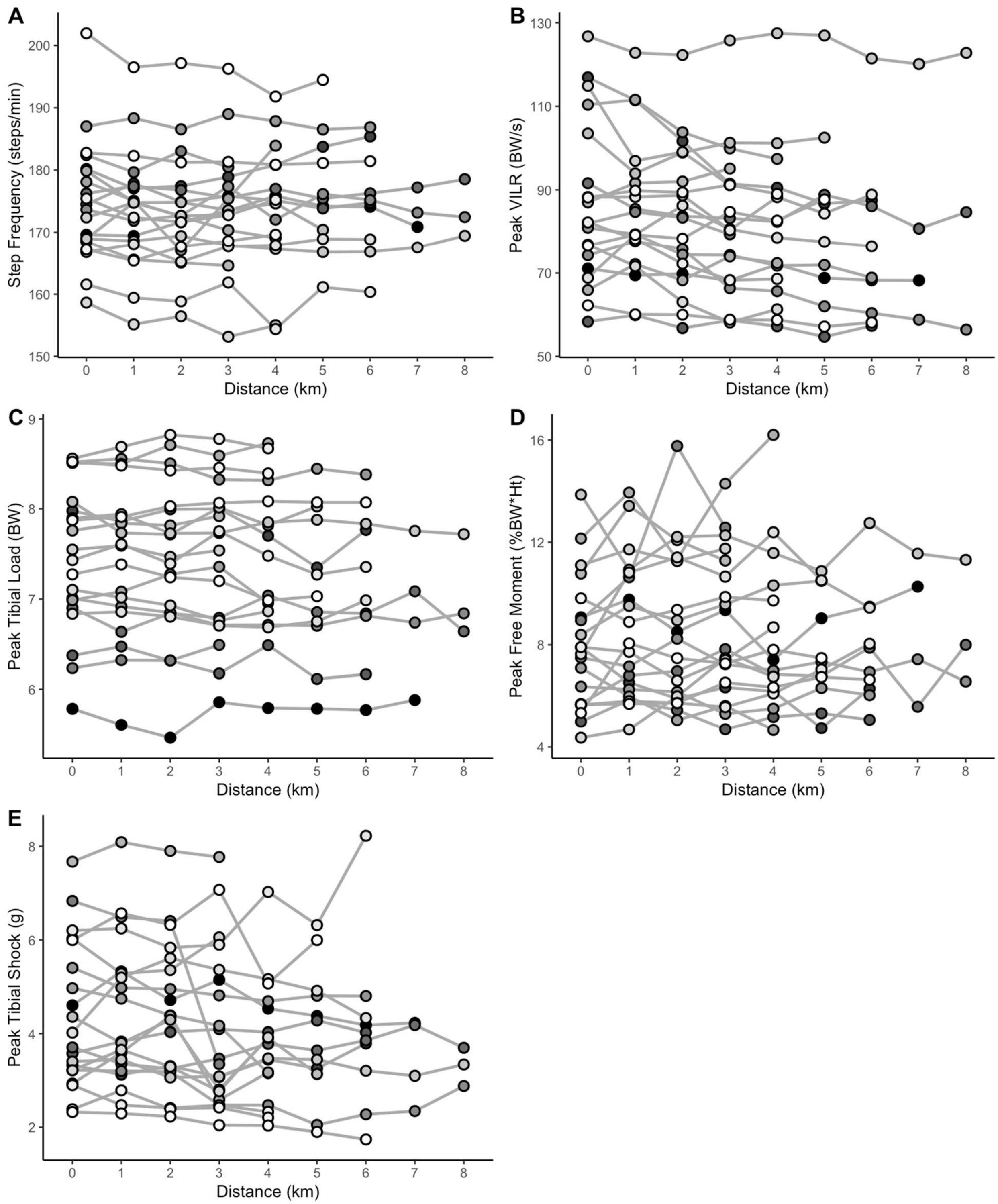

Figure 4.2. Gait mechanics outcomes for each participant at each kilometer they completed. Participants completed between 3 and 8 kilometers.

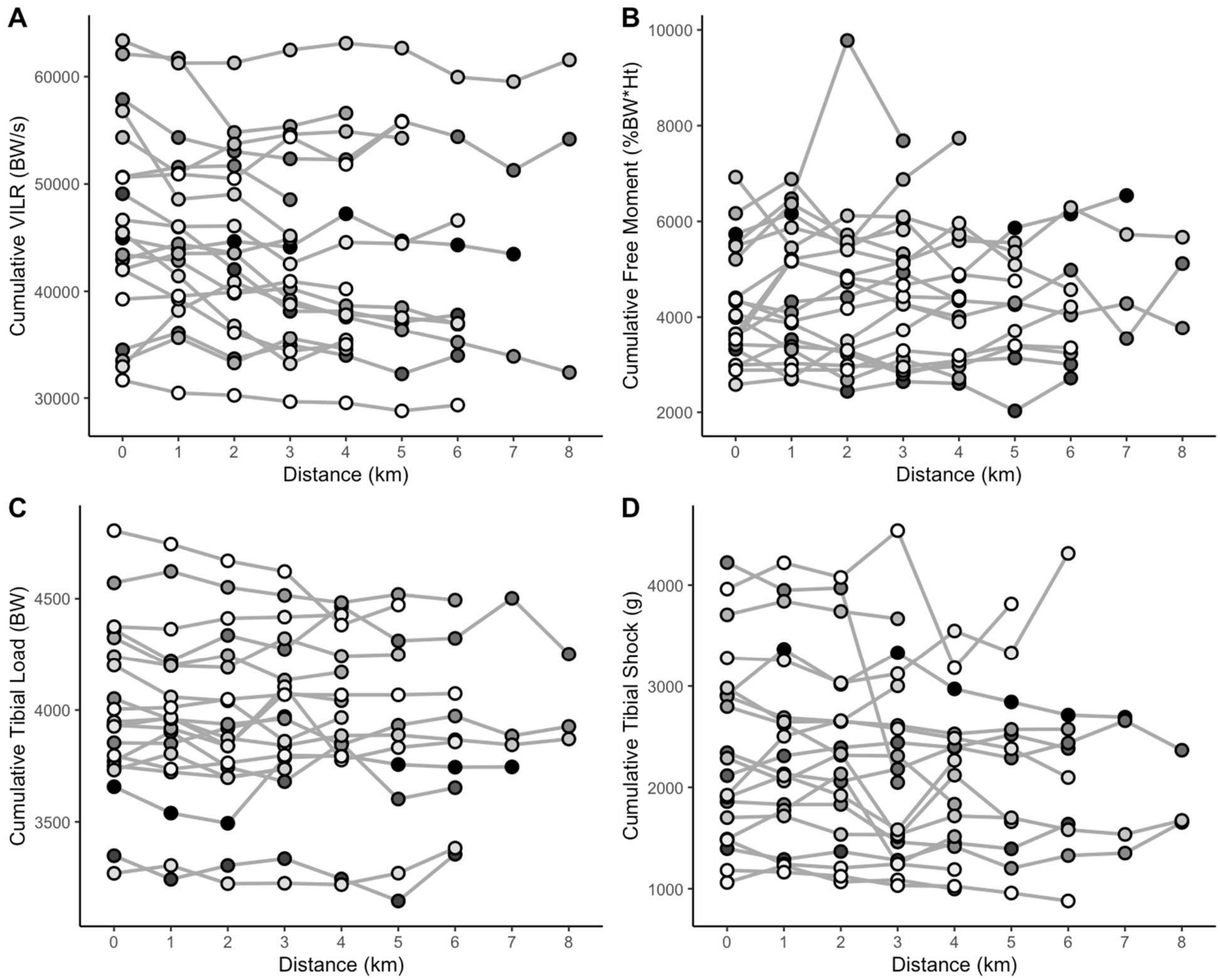

Figure 4.3. Cumulative loads for each participant at each kilometer they completed. Participants completed between 3-8 kilometers.

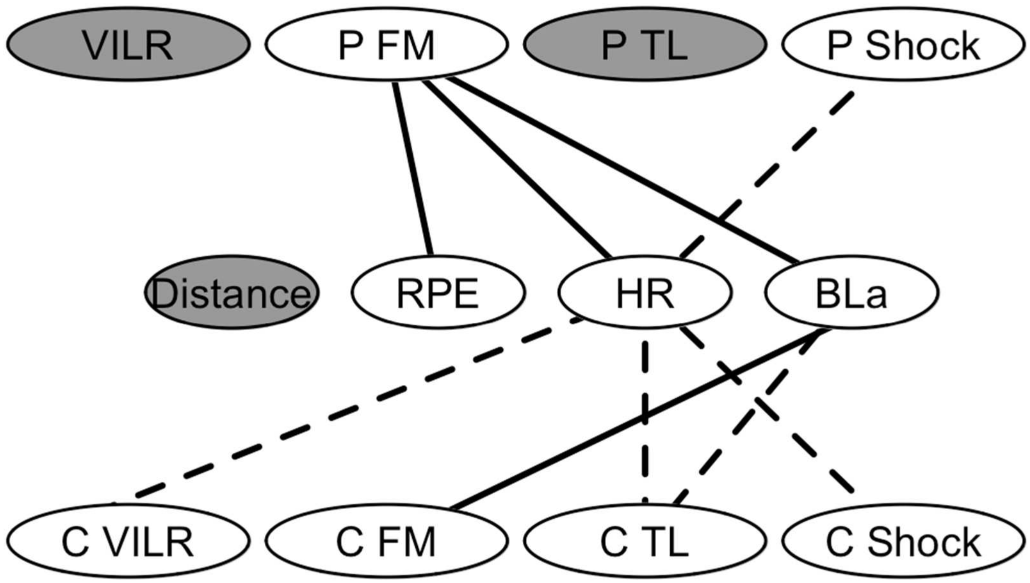

Figure 4.4. A summary of results of correlation tests between loading and performance fatigability outcomes. *Top row:* peak vertical instantaneous loading rate, peak free moment, peak tibial load, peak tibial shock. *Middle row:* Run distance, rating of perceived exertion, heart rate, blood lactate accumulation. *Bottom row:* cumulative vertical instantaneous loading rate, cumulative free moment, cumulative tibial load, cumulative tibial shock. **Solid black lines** indicate positive correlations, **dashed lines** indicate negative correlations. Gray ellipses indicate variables that did not correlate with any other variable.

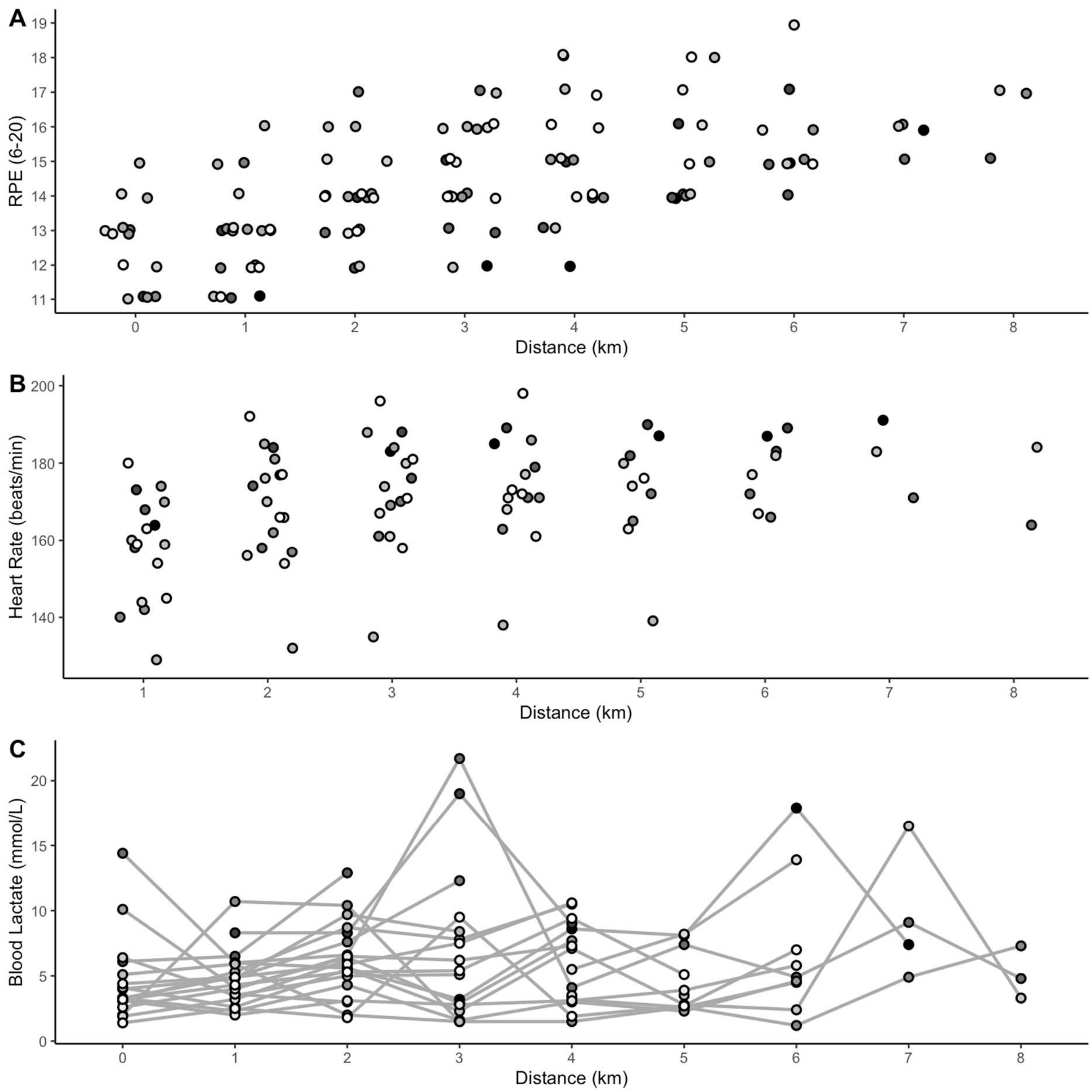

Figure 4.5. Borg Scale Rating of Perceived Exertion (A), average heart rate (B), and blood lactate concentration (C) at the beginning of the run (minute 3) and at the end of each completed kilometer.

Chapter 5: Fatigue does not increase stress fracture risk in runners

Introduction

Injury rates in endurance runners are estimated to be nearly 66% (Kluitenberg et al., 2015; Malisoux et al., 2015; Napier et al., 2018; Nielsen et al., 2014), and stress fractures accounted for up to 21% of all reported running injuries (Battaloglu, 2011; Hespanhol Junior et al., 2012; Kluitenberg et al., 2015). Stress fractures are arguably one of the more serious running related injuries and treatment may require complete cessation of activity, physical therapy, surgery, and long healing times, along with slow reintroduction to activity (Warden et al., 2014). Predictive statistical modeling of tibial stress fracture injury probability suggests that injury risk is highest between 1 to 2 months of beginning a new sport activity (Edwards et al., 2010; Taylor & Kuiper, 2001). Prospective studies and retrospective surveys on training habits and injuries support this finding: novice runners had more than twice the injury incidence than recreational runners per 1000 hours of running (Videbæk et al., 2015) with female runners at the highest risk for stress fracture injuries compared to other female athletes (Battaloglu, 2011).

Until recently, previous studies on running injuries have mostly considered training habits and mechanical loads separately. However, an interaction between these two factors leading to running injuries is likely (Gallagher & Schall Jr., 2017). In materials science, fatigue-failure mechanics refer to the progressive structural changes (cracks or eventual complete fracture) to a material structure resulting from the stresses and strains applied over a sufficient number of loading cycles (Gallagher & Schall Jr., 2017). The cumulative damage of a material is quantified by considering the relationship between various loads applied and the number of loading cycles at each respective load, where lower loads allow for exponentially larger numbers of loading cycles (Gallagher & Schall Jr., 2017). Fatigue-failure mechanics applied to running considers the relationship between the peak loads applied to anatomical structures and the number of steps the structures can withstand before fracturing or tearing (Gallagher & Schall Jr., 2017). "Mechanical fatigue" describes fatigue of this nature. This definition of fatigue differs from the typical endurance sports definition of fatigue, which relates to the decline of physical performance and cognitive perception that occurs during prolonged and/or intense physical activity (Enoka & Duchateau, 2016), and which we will refer to as "performance fatigue."

Performance fatigue during prolonged and/or intense running may cause gait adjustments that contribute to the development of running-related injuries and stress fractures specifically, although a causal relationship between performance fatigue and injury is unclear. Across runners with a wide range of experience, running at varying intensities and durations, performance fatigue had inconsistent effects on temporospatial, kinematic, and kinetic gait outcomes (Clansey et al., 2012; Fischer et al., 2015; Jafarnezhadgero et al., 2019; Maas et al., 2018; Paquette & Melcher, 2017; Willson & Kernozek, 1999). Regarding stride length and tibial load specifically, performance fatigue typically results in a decrease in stride length (Fischer et al., 2015; Willson & Kernozek, 1999), but how performance fatigue affects peak tibial load is not well understood. One study found similar ankle moments before and after a fatiguing run in two different shoe conditions (Jafarnezhadgero et al., 2019) and since muscle forces contribute to a large proportion of the axial tibial force (Matijevich et al., 2019) it is possible that tibial load was also similar. Predictive statistical models combined with finite element estimates of bone strain showed lower tibial stress fracture probability as strides length and peak tibial load decreased concomitantly at a constant running speed (Edwards et al., 2009) and greater stress fracture risk as stride length and peak tibial load increased as running speed increased (Edwards et al., 2010). The results of Edwards et al. (2009, 2010) suggest that a fatigue-induced decrease in stride length associated with a constant or increasing tibial load may increase stress fracture risk. However, how prolonged running affects peak tibial load in novice female runners throughout a run is unknown. Understanding how female novice runners adjust gait in response to prolonged running, and how these adjustments affect stride length and peak tibial load is important for understanding stress fracture injury risk in this population; for example, clarifying if fatigue-related adjustments in running gait mechanics are potentially injurious, protective, or inconsequential for mechanical fatigue of bone.

Therefore, the purpose of this study was to model performance fatigue effects on cumulative damage and probability of tibial stress fracture due to fatigue-related gait adjustments throughout a prolonged run in novice female runners. Performance fatigue during running has been shown to cause decreases in stride length (Fischer et al., 2015; Willson & Kernozek, 1999) and have little effect on ankle moments (Jafarnezhadgero et al., 2019). Therefore, the hypothesis is that the measured fatigue-adjusted gait will result in greater cumulative damage and probability of tibial stress fracture injury due to an increase in the number of loading cycles compared to a hypothetically maintained gait condition. A secondary purpose was to determine if running longer distances is associated with a greater risk of injury, indicated by an increased probability of failure due to performance fatigue. The hypothesis is that longer distances will be associated with a higher ratio between measured fatigue-adjusted and hypothetically maintained gait conditions.

Methods

Experimental Procedures

Joint kinematics and ground reaction forces were collected from 20 healthy, novice female runners (25 ± 6 years old, 16 ± 9 months running experience, running 12.7 ± 6.1 miles per week for ≥3 months). Briefly, participants ran to fatigue at a self-selected speed on an instrumented treadmill, and 16 seconds of gait mechanics were collected at minute 2:45 and during the last ~16 seconds of each kilometer until participants chose to stop. Additional details of the experimental protocol have been described previously (Dissertation Chapter 4). Joint angles and moments were calculated using standard inverse dynamics routines in Visual3D software (C-Motion, Inc., Germantown, MD, USA) (Dissertation Chapter 4). Axial tibial load was calculated by first estimating Achilles tendon moment arm length as 20% of measured foot length. Then the plantarflexion ankle moment during stance was divided by the moment arm estimate to calculate Achilles tendon force. Lastly, the Achilles tendon force was added to the axial component of the resultant ankle force, with the tibial load also expressed on the long axis of the tibia. The tibial load was calculated using an average of 22 steps for the beginning of the run and each kilometer completed, and used in subsequent analysis.

Cumulative Damage and Failure Probability Model Development

This cumulative damage model is based on a theoretical model which applied fatigue-failure mechanics concepts to predict failure of human long bone under cyclic loading (Taylor et al., 2004; Taylor & Kuiper, 2001) and applies these concepts similarly to a previous investigation on cartilage damage and probability of failure (Wasser, Acasio, Hendershot, & Miller, 2020) The relationship between the numbers of loading cycles (strides taken during running) the tibia could withstand is described as:

$$N_f = \frac{C}{\sigma^n} \qquad [5.1]$$

where C = is a constant (Carter et al., 1981), σ = stress, and n = the slope of the linear portion of the S-N curve (Chen et al., 2016; Edwards et al., 2009; Taylor et al., 2004). Since the tibia experiences a range of stresses due to varying ground reaction force peaks and bone geometry, a weighed average of the stress levels applied to the bone is calculated to define a constant-amplitude cycle that would do an equivalent amount of damage as the variable amplitude stresses (Taylor & Kuiper, 2001). This equivalent stress is calculated as:

$$\sigma_{eq} = \left(\frac{1}{N_T}\sum_{i=1}^{j}(N_i\sigma_i^n)\right)^{1/n} \qquad [5.2]$$

where σ_i = peak stress of loading cycle i, j = number of different stress levels, N_i = the number of loading cycles at σ_i, and N_T = the total number of loading cycles over all stresses. Because we are interested in the response of the tibia over a period of days rather than number of loading cycles, we use Equation 5.3 to describe the number of days to failure (t_f). Calculating t_f incorporates Equation 5.1 and the number of loading cycles per day (N_D) determined from a daily run distance D and the stride length L $(N_D = D/L)$ (Taylor et al., 2004):

$$t_f = \frac{N_f}{N_D} = \frac{N_f L}{D} = \frac{CL}{\sigma^n D} \qquad [5.3]$$

Equation 5.3 assumes that cyclic loading applied daily over a number of loading cycles leads to a daily amount of damage that accumulates until failure on day t_f. We can determine the number of loading cycles N over any time period t again using a daily run distance D and stride length L $(N = tD/L)$. Then we use this N, and substituting the formulas for N_f from Equation 5.1 and t_f from Equation 5.3 to calculate the fraction of cumulative damage on day *t:*

$$\delta = \frac{N}{N_f} = \frac{t}{t_f} = \frac{tD\sigma^b}{aL} \qquad [5.4]$$

To calculate the probability of failure (P_f), Taylor & Kuiper (2001) proposed a modified Weibull equation to estimate the fatigue life of different sections of the tibia where different stresses are applied:

$$P_f = 1 - \exp\left[-\left(\frac{V_s}{V_{so}}\right)\left(\frac{\sigma}{\sigma^*}\right)^m\right] \qquad [5.5]$$

where V_s = volume of individual sections of bone, V_{so} = a reference volume of bone, σ^* = the stress range for P_f = 0.63, and m = the degree of scatter in the data (Taylor & Kuiper, 2001). By solving for σ from Equation 5.5, we can substitute it in Equation 5.6 to determine the probability of failure given uncertainty in subject-specific bone stresses and stress-life relationships.

$$P_f = 1 - \exp\left[-\left(\frac{V_s}{V_{so}}\right)\delta^{m/b}\right] \qquad [5.6]$$

Accurately estimating individual bone stresses during running requires invasive procedures that are not currently feasible, or costly and complex modeling that requires bone volume and geometry models created from CT scans. In order to simplify estimates of damage we attempted to simplify calculations of cumulative damage and failure probability using standard gait mechanics analysis outcomes. Calculating the ratio of cumulative damage and failure probability between two running conditions, non-fatigued versus fatigued, causes unknown values such as individual bone volume and bone fatigue life to be unnecessary in the model. To use Equations 5.1-5.6 with standard gait analysis data, we assume the axial tibial loads are proportional to bone stresses, and forces are applied to equal bone volumes in the non-fatigued and fatigued conditions. Stride length (L_{NF}) and tibial load (TL_{NF}) for the non-fatigued condition were the stride length and tibial load estimated at the end of the first 3 minutes of running. To describe the step length (L_F) and the tibial load (TL_F) for the fatigued condition, an equivalent stride length and tibial load were calculated for each participant based on the total number of kilometers *k* they completed using Equations 5.7 and 5.8, respectively, following the similar definition from Eq. 5.2:

$$L_F = \sum_1^k (N_i \cdot L_i) / \sum_1^k N_i \qquad [5.7]$$

$$TL_F = \sum_1^k (N_i \cdot TL_i^n) / \left(\sum_1^k N_i\right)^{1/n} \qquad [5.8]$$

where N_i is the number of strides at kilometer *k*, TL_i is the tibial load at kilometer *k*, and n = 6.6 (Carter et al., 1981). We then use a modification of Equation 5.3 to calculate the damage ratio of fatigued versus non-fatigue over an equal distance, for example over one kilometer:

$$\frac{\delta_F}{\delta_{NF}} = \left(\frac{L_{NF}}{L_F}\right)\left(\frac{TL_F}{TL_{NF}}\right)^n \qquad [5.9]$$

Equation 5.1 can be modified to estimate the number of strides of non-fatigued running that equal the damage from a single stride of fatigued running:

$$\frac{N_{NF}}{N_F} = \left(\frac{TL_F}{TL_{NF}}\right)^C \qquad [5.10]$$

We expressed the failure probability ratio as the log-probability of not failing, so the ratio of log-probabilities between fatigued and non-fatigued is:

$$\frac{\ln(1-P_{fF})}{\ln(1-P_{fNF})} = \left(\frac{L_{NF}}{L_F}\right)^{C/n}\left(\frac{TL_F}{TL_{NF}}\right)^C \qquad [5.11]$$

For Equations 5.9 and 5.11, a ratio of > 1.0 indicates an increase cumulative damage and probability of failure, respectively, due to measured fatigued-adjusted gait over the course of a run compared to a hypothetical condition where gait was maintained throughout the run, while a ratio of < 1.0 suggests the opposite.

Statistical Analysis

Statistical analysis was performed using a customized script in R (Team, 2020). To determine whether a change in the number of loading cycles or a change in tibial load led to any potential fatigue effects, comparisons were made between non-fatigued step length and tibial load and fatigued condition equivalent step length and equivalent tibial load, calculated for each participant from Equations 5.7 and 5.8.

The damage ratios calculated from Equations 5.9-5.11 were compared to a null effect of fatigue, or a ratio of 1. All variables were assessed for normality (Shapiro-Wilk Test) and homogeneity of variance (Levene's Test). No variables passed both tests, therefore two-sided Welch's unequal variances *t*-test was used for all comparisons. Cohen's *d* effect sizes were calculated to measure the size of effects with 0.2, 0.5, and 0.8 showing small, medium, and large effects, respectively.

Spearman's rho was calculated to determine the relationship between run distance and probability of fracture ratios, which may indicate if longer running distances were associated with greater effects of performance fatigue on failure probability.

Results

Participants ran at an average treadmill speed of 6.1 mph (2.7 m/s) and completed an average of 5 kilometers (range: 3-8 km). Additional details of participant demographics and running outcomes can be found in Table 5.1. When comparing the measured fatigue-adjusted and hypothetically maintained gait conditions, both stride lengths and tibia loads were similar (Table 5.2).

The ratios of cumulative damage (0.98), damage per stride (0.99), and probability of failure (0.99) between measured fatigue-adjusted and hypothetically maintained gait conditions were not significantly different compared to a null effect of fatigue (Table 5.2). Individual results varied for each ratio calculated and are shown in Figure 5.1.

There was a moderate, negative relationship between run distance and probability of fatigue ratio, however this relationship was not quite statistically significant ($r_s = -0.44$, $p = 0.051$) (Figure 5.2).

Discussion

The purpose of this study was to model performance fatigue affects on cumulative damage and probability of tibial stress fracture due to fatigue-related gait adjustments throughout a prolonged run in novice female runners. We hypothesized that gait adjustments due to fatigue would increase the cumulative damage and probability of tibial stress fracture injury due to an increase in the number of loading cycles and due to the common suspicion in running science that fatigue is a source of injury. This hypothesis was not supported. Rather than a decrease in stride length in the measured fatigue-adjusted gait condition as we expected, stride lengths were similar in hypothetically maintained and measured fatigue-adjusted gait conditions (Table 5.2). The number of strides of hypothetically maintained gait that equal measured fatigue-adjusted gait, and the ratios of both damage per kilometer and probability of failure between measured fatigue-adjusted and hypothetically maintained gait conditions, were also similar to a null effect of fatigue (Table 5.2).

The secondary purpose of this study was to determine if running longer distances is associated with a greater ratio of probability of failure between measured fatigue-adjusted and hypothetically maintained gait conditions. The hypothesis that longer run distances would be associated with greater fatigue-related gait adjustments and therefore a greater probability of failure compared to the hypothetically maintained gait condition was not supported. There was a moderate, but non-significant negative relationship between run distance and the probability of failure ratio (Figure 5.2).

The present model assumes that tibial loads estimated from inverse dynamics accurately represent the stress applied to the bone during running. It is possible to more rigorously estimate the probability of failure of bone using complex modeling techniques that combine inverse dynamics, muscle modeling, finite element modeling, and predictive statistical modeling, and these techniques have been used in several studies to estimate bone stress/strain and/or injury probability under various conditions (Chen et al., 2016; Edwards et al., 2009, 2010; Taylor et al., 2004; Taylor & Kuiper, 2001). Although the methods of the aforementioned studies were more complex than the current study, the results support our findings. Specifically, longer stride lengths were associated with greater tibial contact force and greater probability of fracture at a constant running speed (Edwards et al., 2009) and as running speed increased (Edwards et al., 2010). In addition, alterations in foot strike pattern while running at a constant cadence increased ankle joint contact force but did not lead to significantly different peak tibial strain or probability of failure (Chen et al., 2016). Taken together, the results of Edwards et al. (2009, 2010) and Chen et al. (2016) support our findings that the similar stride lengths and peak tibial loads we estimated throughout a run would lead to similar cumulative damage and probability of failure. However, in cases where axial loads increase significantly, there is a potential risk of overestimating probability of failure using our method, since one study showed that axial loads increased while peak tibial strain did not (Chen et al., 2016). We also did not include other daily physical activity such as walking or stair climbing, or estimates of adaptation and repair that are incorporated into other predictive models (Chen et al., 2016; Edwards et al., 2009, 2010; Taylor et al., 2004). Since we calculated and reported only the ratios between measured fatigue-adjusted and hypothetically maintained gait conditions, equal amounts of additional activity, and the short- and long-term bone response would appear in both the numerator and denominator of these equations and not affect the results. In addition, modeling the probability of fracture using more complex methods may not necessarily provide more accurate results. A comparison of finite element models of different complexity resulted in highly variable results where only the most complex model corresponded to in vivo outcomes, and the more commonly used models either overestimated bone deformation or predicted bone deformation in the wrong direction (Haider, Baggaley, & Brent Edwards, 2020). Although there is a risk of overestimating cumulative damage and the probability of failure using our model, it is also possible that a method to adjust the tibial loads to more accurately represent the associated tibial strains could be developed for use in future iterations, as other common gait mechanics outcomes have been weighted to accurately predict injury using cumulative training load estimates (Kiernan et al., 2018). Future investigations determining the relationship between tibial load and tibial strain during running could contribute to improved accuracy of the current model.

We expected a shorter stride length in the measured fatigue-adjusted gait condition compared to the hypothetically maintained gait condition, however the stride lengths were similar. The response of kinetic and kinematic outcomes to fatigue during running is inconsistent and therefore difficult to predict (Clansey et al., 2012; Fischer et al., 2015; Gerlach et al., 2005; Jafarnezhadgero et al., 2019; Maas et al., 2018; Paquette & Melcher, 2017; Verbitsky et al., 1998; Willson & Kernozek, 1999). It is possible that other potential injury-related variables we did not measure were modified due to fatigue, such as GRF characteristics, joint kinetics, joint kinematics, or tibial acceleration, since these variables have previously been shown to alter with fatigue without a reported change in temporospatial outcomes (Clansey et al., 2012; Jafarnezhadgero et al., 2019; Maas et al., 2018; Paquette & Melcher, 2017). It is also possible that sex and running experience may influence gait mechanics in general, and in turn, the response of gait mechanics to fatigue. A mixed-sex group of runners with varying experience were classified as male/female and recreational/competitive based only on center of mass acceleration characteristics during running (Clermont et al., 2019). In response to a fatiguing run, well-trained female and male runners showed a respective decrease and increase in peak loading rates of the GRF (Clansey et al., 2012; Gerlach et al., 2005). Novice female runners altered lower extremity kinematics more than experienced female runners (Maas et al., 2018) and exhibited increased knee sagittal and transverse plane moments and increased hip sagittal plane moments (Jafarnezhadgero et al., 2019) in response to fatigue. In addition, menstrual cycle and oral contraception affected tibial acceleration during running (Clark, Bartold, & Bryant, 2010). This is important especially for female runners because studies that have found increases in tibial acceleration with no change in step length suggest that fatigue-related adjustments at the knee that prevent a change in step length may also contribute to injury risk (Derrick et al., 2002; Gerlach et al., 2005).

Additional limitations to this study involve the challenge of defining both a novice runner and running fatigue as previous studies on running injuries have used different definitions of both. Studies of novice runners have required lifetime running experience from no specified minimum (Chan et al., 2018; Maas et al., 2018) to a minimum of 3 months (Napier et al., 2018), and up to either 2 years (Chan et al., 2018), 3 years (Maas et al., 2018), or no specified maximum (Napier et al., 2018). These requirements often overlap with definitions of recreational runners, which required only 6 months of experience (Fischer et al., 2015) or no specified running experience at all (Verbitsky et al., 1998). The amount of running exposure for novice runners also varies from a minimum of 8 kilometers per week (Chan et al., 2018), 10 kilometers per week (Maas et al., 2018), or runners who completed a maximum of 2 half-marathons (Napier et al., 2018). This level of exposure also overlaps somewhat with that of recreational runners, where exposure of 2-3 times per week with one sessions of at least 45 minutes (Jafarnezhadgero et al., 2019) or at least 30 kilometers per week were required (Fischer et al., 2015). Our inclusion criteria overlapped with the definitions of novice and recreational runners since we required 3 months to 2 years of lifetime running experience, an exposure of at least 8 kilometers per week over 3 consecutive months prior to participation, and have no competitive running experience, but did not define specific maximum running exposures or limit other exercise modalities (Dissertation, Chapter 4). A recent study addressed this lack of common definitions of running experience/exposure in research, proposing definitions of 3 levels of runners: novice, recreational, and high-caliber (Honert, Mohr, Lam, & Nigg, 2020). According to their criteria, our participants fell somewhere between novice and recreational levels of experience and exposure, however these classifications should be applied to female populations with caution as they also include performance metrics that apply only to males (Honert et al., 2020). More agreement between studies on whether runners are novice, recreational, experienced, or otherwise will improve applicability of study results to specific populations of runners. Runner experience, exposure, performance, and participation in planned physical exercise other than running is important since these factors may influence running capacity, and we found that runners who were able to complete longer distances had smaller ratios between hypothetically maintained gait and measured fatigue-adjusted gait conditions (Figure 2).

The protocols used in running fatigue studies also vary widely. Some studies have required runners to reach exhaustion (Jafarnezhadgero et al., 2019; Maas et al., 2018; Willson & Kernozek, 1999) while other have required longer-duration runs at or near threshold (Clansey et al., 2012; Verbitsky et al., 1998) or even lower relative intensity (Paquette & Melcher, 2017). Other fatigue studies have used localized muscle fatigue protocols (Fischer et al., 2015), although we generally focus our comparisons to studies that used running as the source of fatigue. We chose a submaximal protocol most similar to Paquette & Melcher (2017) where runners ran at their self-selected long run pace, although in our study we allowed them to decide when to cease running rather than define a predetermined distance. The goal of the protocol in this study was to recreate conditions runners experience during their longest weekly run. It is possible that runners did not experience sufficient levels of fatigue to elicit substantial gait adjustments that affect cumulative damage of the tibia and subsequent probability of failure. In applying these results to typical training durations and intensities, our results suggest that novice runners are able to determine appropriate distances for their capacity without substantially increasing their risk of injury within a single run. However, whether novice runners maintain gait mechanics when running unusual distances, such as when undertaking training for a new race distance, is unclear. In addition, a lack of fatigue effects in a single run does not account for the potential effects of fatigue from the training load of multiple days or weeks of running that may contribute to injury risk over a training period (Kiernan et al., 2018). Whether consecutive days of training, including training at relatively low intensities, contribute to fatigue-related gait adjustments is unknown. Future studies investigating the effects of consecutive days of training on fatigue-related gait adjustments would improve understanding of how training habits beyond simply running speed and distance may contribute to injury risk.

In conclusion, when novice female runners ran at a steady self-selected pace to fatigue, the measured fatigue-adjusted gait condition stride length and tibial load estimated from all completed kilometers were similar to the hypothetically maintained gait stride length and tibial load estimated at the beginning of the run. The ratios of measured fatigue-adjusted gait versus hypothetically maintained gait condition cumulative damage and probability of failure were also not significantly different from a null effect of fatigue, and the amount of damage estimated to occur from a single hypothetically maintained gait stride was similar to that of a measured fatigue-adjusted gait stride. These results suggest that runners choose to stop running prior to experiencing substantial adjustments in gait mechanics, and fatigue related changes in gait mechanics during an ‘easy’ run are not likely a major injury risk factor at least from the perspective of a “cumulative damage” theory on injury causation. We also found a moderate but non-significant negative relationship between self-selected run distance and probability of failure ratio, which suggests that runners who are able to comfortably run longer distances may maintain gait mechanics better than those who can only complete short distances. However, we used a simple model to compare the cumulative damage and probability of failure between measured fatigue-adjusted and hypothetically maintained gait conditions during a single easy run. Examining how our simple model estimates compare to more complex model estimates, if and how our model inputs could be tuned to accurately correspond to in vivo responses, as well as if fatigue over a period of training affects injury risk factors is worthwhile.

Table 5.1

Participant Characteristics

	mean (SD)	Range
Age (years)	25 (6)	18-38
Height (cm)	165.2 (6.9)	150.9-176.4
Mass (kg)	64.0 (10.3)	43.3-84.9
Running Experience (months)	16 (9)	3-8
Running Exposure (miles/wk)	12.7 (6.1)	4.5-25
Run Speed (mph)	6.1 (0.7)	5.0-8.0
Run Distance (km)	5 (1.6)	3-8

Table 5.2

Model Inputs and Calculated Ratios

		mean (SD)	Range	*p*	Cohen's *d*
Stride Length (m)	Hypothetically Maintained Gait	1.88 (0.23)	1.51-2.38	0.231	0.04
	Fatigue-Adjusted Gait	1.90 (0.23)	1.56-2.38		
Tibial Load (BW)	Hypothetically Maintained Gait	7.46 (0.81)	5.78-8.56	0.430	0.02
	Fatigue-Adjusted Gait	7.44 (0.82)	5.75-8.71		
Ratios	Cumulative Damage	0.98 (0.09)	0.83-1.14	0.349	0.29
	Damage Per Stride	0.99 (0.10)	0.83-1.15	0.596	0.21
	Failure Probability	0.99 (0.04)	0.92-1.06	0.294	0.33

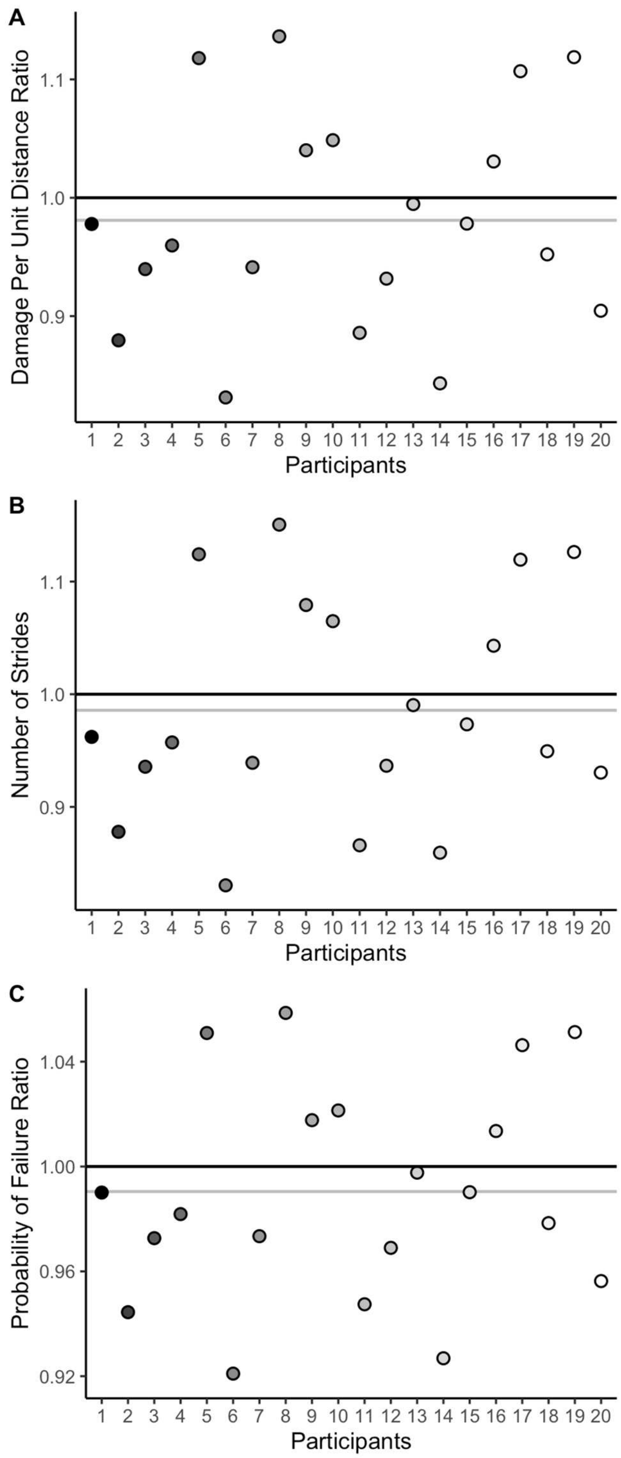

Figure 5.1. Cumulative damage ratio of measured fatigue-adjusted gait versus hypothetically maintained gait per unit distance (A), the number of hypothetically maintained strides that equal measured fatigue-adjusted strides (B), and probability of failure in measured fatigue-adjusted versus hypothetically maintained gait (C). Black horizontal lines demarcate between greater (ratios > 1.0) and lesser (ratios < 1.0) damage/probability of failure. Gray horizontal lines indicate the mean ratios for all participants.

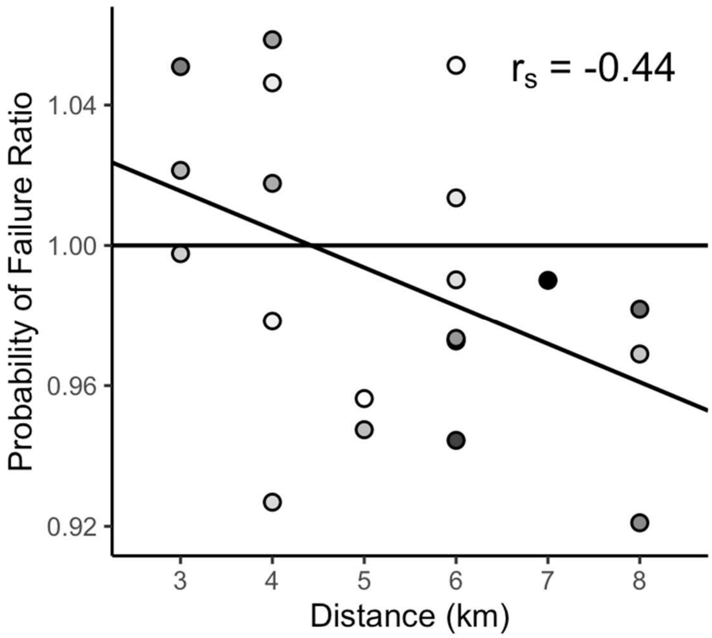

Figure 5.2. The relationship between run distance and probability of failure ratio. Although there was a moderate relationship showing that the probability of fatigue ratio decreased with longer run distances, it was not significant ($p > 0.05$).

Chapter 6: Conclusion

Summary

The overall objective of this dissertation was to investigate how training habits affect cumulative load and tibial stress fracture injury risk in runners. Estimating cumulative load, cumulative damage, and probability of failure applies fatigue-failure concepts from materials science, which is a relatively new research paradigm applied to running injury biomechanics. The studies that comprise this dissertation applied these concepts by i) estimated the cumulative load of two proportions of running speed over a constant distance and average pace of running; ii) estimated how fatigue-related gait adjustments affect the loads accumulated per-kilometer within a single prolonged run, and if there is a relationship between gait adjustments and either physiological or cognitive fatigue outcomes; and iii) estimated if fatigue-related gait adjustment affected cumulative damage or the probability of failure of the tibia compared to no effect of fatigue. Chapter 3 investigated how the easily modifiable factor of running speed affects the loads accumulated over a set distance, since running injuries are often attributed to too much fast running. Chapter 4 investigated how fatigue-related gait adjustments affected estimates of per-kilometer cumulative loads associated with tibial stress fractures over a steady-state run to fatigue. This chapter also included exploratory investigations of the associations between peak loads, cumulative loads, and easy to measure physiological and cognitive outcomes. Chapter 5 compared the cumulative damage and probability of failure of the tibia between measured fatigue-adjusted gait and hypothetically maintained gait mechanics. Chapter 1 of this document presented the formal hypotheses associated with each chapter, and the hypotheses, results, and conclusions of each study were addressed in their respective chapter and are summarized here.

Chapter 3

The first hypothesis was that running all distance at a self-select 'normal' speed and running the same distance at the same average speed using a combination of self-selected 'slow' and 'fast' speeds would have similar estimated cumulative VALR, free moment, and tibial load, and that the slow and fast speed would contribute similarly to the total cumulative load of the slow and fast combination. This hypothesis was partially supported: estimated cumulative free moment and tibial load were similar between the two speed distributions; however, estimated cumulative VALR was significantly lower when all mileage was run at normal speed compared with the combination of slow and fast speed.

The second hypothesis was that slow and fast speeds would contribute similarly to the total cumulative load of the combined slow and fast condition. This hypothesis was also partially supported: slow and fast speeds contributed similarly to estimated cumulative VALR and free moment, but slow running had a significantly greater contribution to estimated cumulative tibial load than fast running. In summary, volume and average pace may not be sufficient metrics for tracking cumulative load when speed fluctuates substantially over the course of a training volume or within a single run.

Cumulative load has a compelling theoretical basis for playing a causal role in tissue damage and failure, however there are currently no known relationships between high or low values of any particular cumulative biomechanical load and the risk for any particular running injuries. Prospective studies from different labs have shown inconsistent results between studies concerning which peak loads per step are associated with injury, and while assessments of cumulative loads would not necessarily show more consistent results the possibility seems worthwhile of investigation. Additionally, the results do not account for potential within-run or between-run changes in running mechanics, muscle/tendon mechanics, structure-specific capacity, or metabolic factors that may cause changes in cumulative loads experienced by runners within a run or as they perform runs over a period of training.

Chapter 4

The first hypothesis of study 2 was that cumulative loads per kilometer would increase during the run due to a fatigue-related increase in step frequency. This hypothesis was not supported. Since step frequency and peak loads were both maintained throughout the run there was no effect of run distance on cumulative loads per kilometer.

The second hypothesis was that HR and RPE would positively correlate with cumulative loads per kilometer but not peak loads, and there would be no relationship between blood lactate accumulation and peak loads or cumulative loads per kilometer. No per-kilometer cumulative load variables were positively correlated to RPE or HR. Rather, cumulative VILR, cumulative tibial load, and cumulative shock were negatively correlated to HR and there was no relationship between any cumulative loads per kilometer and RPE. In addition, we found that peak free moment was positively correlated to RPE and HR, and peak tibial shock was negatively correlated to HR. We also found that peak free moment and cumulative free moment were positively correlated to blood lactate accumulation, and cumulative tibial load was negatively correlated to blood lactate accumulation.

In summary, when novice female runners ran at a steady self-selected pace to fatigue, step frequency, cumulative VILR, cumulative free moment, cumulative tibial load, and tibial shock remained similar throughout the run. These results suggest that runners choose to stop running prior to experiencing altered gait mechanics. The present results also suggest that fatigue-related changes in gait resulting in increased peak or cumulative loads in the latter kilometers of 'easy' runs are not likely a major injury risk factor. In addition, tracking HR and tibial shock may be an effective way to determine the onset of fatigue during outdoor training runs.

It is possible that runners did not reach sufficient fatigue to elicit changes in gait mechanics. However, this condition is consistent with our goal of measuring a run that represents the majority of a participant's "typical" running, where they are presumably not running to utter exhaustion very often. In addition, differences between the lab environment and runners' true running environment may have influenced the loads runners accumulated. It remains to be seen if monitoring "real-world" cumulative loads, e.g. via wearable devices, provides useful information for predicting/explaining/preventing injuries in runners.

Chapter 5

Building on the findings of the prior chapter, this chapter examined if fatigue during an easy run influenced estimated tibial stress fracture risk. The first hypothesis was that gait adjustments due to fatigue would increase the cumulative damage and probability of tibial stress fracture injury due to an increase in the number of loading cycles. This hypothesis was not supported. We found that the ratio of damage per kilometer, the number of strides of non-fatigued running that equal fatigued running, and the ratio of probability of failure between hypothetically maintained gait and fatigue-adjusted gait conditions were similar to a null effect of fatigue. The second hypothesis was that longer distances would be associated with greater fatigue and therefore a greater ratio of the probability of failure of the measured fatigue-adjusted gait versus the hypothetically maintained gait condition. This hypothesis was also not supported. There was a moderate, but non-significant negative relationship between run distance and the probability of failure ratio. In summary, when novice female runners ran at a steady self-selected pace to fatigue, the measured fatigue-adjusted gait condition stride length and tibial load estimated from all completed kilometers were similar to the hypothetically maintained stride length and tibial load estimated at the beginning of the run. The ratios of hypothetically maintained versus measured fatigue-adjusted gait condition cumulative damage and probability of failure were also not significantly different from a null effect of fatigue, and the amount of damage estimated to occur from a single hypothetically maintained gait stride was similar to that of a measured fatigue-adjusted stride.

These results suggest that runners choose to stop running prior to experiencing substantial adjustments in gait mechanics, and fatigue related changes in gait mechanics during an 'easy' run are not likely a major injury risk factor. However, the present model assumes that tibial loads estimated from inverse dynamics accurately represent the stress applied to the bone during running. It is possible that a more rigorous estimate of the probability of failure of bone using complex modeling techniques combining inverse dynamics, muscle modeling, finite element modeling, and predictive statistical modeling may detect differences that the present model did not. It is also possible that sex and running experience may influence gait mechanics in general, and in turn, the response of gait mechanics to fatigue.

General Conclusions

The findings of this dissertation argue against some commonly suspected notions of injury causation in runners: (i) that runners accumulate more loads from large proportions of fast running versus moderate or slow running, and (ii) that fatigue-related gait adjustments in the latter kilometers of 'easy' runs is a major injury risk factor. These findings suggest that while the cumulative load of slow, easy runs may be higher compared to fast speeds, runners are able to maintain gait mechanics at slow speeds such that the cumulative damage and risk of injury during these runs is relatively constant. These findings contribute to better understanding of how fatigue-failure concepts from materials science may be applied to running injury biomechanics, and establish a basis for future research to investigate how different training speeds and/or volumes affect cumulative load, cumulative damage, and stress fracture injury risk.

Future Work

The present interpretations about cumulative load of different speed distributions are based on highly controlled speed distributions rather than realistic training programs, and the application of the cumulative damage and the probability of stress fracture injury model was limited to novice runners running at relatively slow speeds in this research. Future investigations into how cumulative load and cumulative damage are affected by factors such as changes in footstrike pattern, changes in running speed, or more extreme levels of fatigue, both within a single run and across a period of training, may further our understanding of how gait mechanics and modifiable training habits affect cumulative load and stress fracture injury risk in runners. In addition, examining how our simple model estimates compare to more complex model estimates, if and how our model inputs could be tuned to accurately correspond to in vivo responses, as well as if fatigue over a period of training affects injury risk factors is worthwhile. When cumulative load estimates are weighted to account for the nonlinear relationship between cumulative loads and cumulative damage, estimates of injury risk from cumulative loading outcomes alone are promising (Kiernan et al., 2018). The results of Kiernan et al. (2018) apply to competitive collegiate male runners, while the present results apply to novice female runners, therefore, more research on how estimates of cumulative load, cumulative damage, and probability of failure apply to different populations of athletes under different training conditions are also warranted.

Appendices

Appendix 1: Derivation of Equation 3.1

1. Begin with the time and distance at normal speed:

$$T = \frac{d_{normal}}{v_{normal}}$$

2. Substitute the proportions of slow and fast distance to equal the same total time:

$$\frac{d_{fast}}{v_{fast}} + \frac{d_{slow}}{v_{slow}} = T$$

3. Replace d_{fast} so there is only one unknown, based on the fact that $d_{normal} = d_{slow} + d_{fast}$:

$$\frac{d_{normal} - d_{slow}}{v_{fast}} + \frac{d_{slow}}{v_{slow}} = T$$

4. Multiply both sides by v_{fast}:

$$d_{normal} - d_{slow} + \frac{d_{slow} v_{fast}}{v_{slow}} = v_{fast} T$$

5. Rearrange the equation so d_{slow} is on one side:

$$\frac{d_{slow} v_{fast}}{v_{slow}} - d_{slow} = v_{fast} T - d_{normal}$$

6. Isolate d_{slow} in 2 steps:

$$d_{slow}\left(\frac{v_{fast}}{v_{slow}} - 1\right) = v_{fast} T - d_{normal}$$

$$d_{slow} = \frac{v_{fast} T - d_{normal}}{\frac{v_{fast}}{v_{slow}} - 1}$$

7. Simplify the denominator:

$$d_{slow} = \frac{v_{fast}T - d_{normal}}{\frac{v_{fast} - v_{slow}}{v_{slow}}}$$

8. Multiply by the inverse of the denominator to simplify the equation to the final version:

$$d_{slow} = \frac{v_{fast}v_{slow}T - d_{normal}v_{slow}}{v_{fast} - v_{slow}}$$

Appendix 2: Study 2 Participant Questionnaire

Demographic Information

Please provide the following information:

Age: __________________ (years, months)

Race:___________________

Dominant leg: ☐ Right ☐ Left
Dominant hand: ☐ Right ☐ Left

Part 1: Running and Exercise History

How long have you been running? *Please indicate in months or years, as appropriate.*

____

On average, how many times a week do you run (over the past 3 months)?
_______________ times/week

On average how many hours do you run per week (over the last 3 months)?
_______________ hours/week

On average how many miles do you run per week (over the last 3 months)?
_______________ miles/week

Please indicate the distances you have raced, and how many. *Check all that apply.*
5 km: How many
10 km: How many
half marathon: How many
full marathon: How many

Do you participate in other exercise?
Yes
No

If yes,
Please provide details of the other activity/activities you participate in as planned exercise/recreation.

Actvity: _______________

On average, how many times a week do you perform this activity (over the past 3 months)?
_______________ times/week

On average how many hours do you perform this activity (over the last 3 months)?
_______________ hours/week

Actvity: _______________

On average, how many times a week do you perform this activity (over the past 3 months)?
_______________ times/week

On average how many hours do you perform this activity (over the last 3 months)?
_______________ hours/week

Actvity: _______________

On average, how many times a week do you perform this activity (over the past 3 months)?
_______________ times/week

On average how many hours do you perform this activity (over the last 3 months)?
_______________ hours/week

Actvity: _______________

On average, how many times a week do you perform this activity (over the past 3 months)?
_______________ times/week

On average how many hours do you perform this activity (over the last 3 months)?
_______________ hours/week

Part 2: Footwear

For the past year, list the brand and model of the running shoes you wear most often during running:
Brand: ______________
Model: ______________
Percent of time spent in shoe: ______________

Is this the running shoe you are wearing today?
☐ Yes ☐ No
If yes,
Estimated mileage: ______________

If no,
Please list the brand and model you are wearing today.
Brand: _______________
Model: _______________
Estimated mileage: _______________

Do you wear another pair of running shoes?
If Yes,
Brand: _______________
Model: _______________
Percent of time spent in shoe: _______________

Part 3: Injury History

In the past year, have you suffered any injuries that affected your ability to walk or run?
Yes
No

In the past year, have you undergone any surgery that affected your ability to walk or run?
Yes
No

If yes,
What surgical procedure did you undergo?

In the past year, have you experienced any major health conditions that affected your ability to walk or run?
Yes
No

If yes,
What condition did you experience?

Part 4: Coronary Artery Disease Risk Stratification

Please mark ALL true statements.

Section 1--*You have had:*

- a heart attack
- heart failure
- cardiac arrhythmia
- known heart murmur
- congenital heart disease
- any heart surgery
- coronary heart surgery
- heart palpitations

Section 2--*You have:*

- experienced unusual chest pain with mild exertion
- experienced unusual dizziness, falling, or blackouts with mild exertion
- experienced unusual fatigue or shortness of breath during usual activities
- been prescribed heart medications
- you are a man older than 45 years or a woman older than 55 years

Section 3--*You have:*

- history of heart problems (heart attack, by-pass surgery, sudden death) in immediate family (before 55 years of age in father or other male 1st degree relative or before 65 years of age in mother or other female 1st degree relative)
- you take blood pressure medication
- you are a diabetic or take medicine to control your blood sugar
- you have high cholesterol >200 mg/dL (or HDL is less than 35mg/dL or LDL is greater than 169 mg/dL)
- you smoke
- your blood pressure is greater than 140/90 mmHg

- None of these apply.

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